EVALUATION OF EFFICACY OF TRANSDERMAL NITROGLYCERINE IN THE TREATMENT OF PRETERM LABOUR

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OBSTETRICS AND GYNAECOLOGY

K.A.P. Viswanathan Government Medical College
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Chennai.

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CERTIFICATE

This is to certify that the dissertation entitled "EVALUATION OF EFFICACY OF TRANSDERMAL NITROGLYCERINE IN THE TREATMENT OF PRETERM LABOUR" is a bonafide work done by **Dr. T. RIZWANA TAJ** at K.A.P. Viswanathan Government Medical College, Trichy. This dissertation is submitted to Tamilnadu Dr. M.G.R. Medical University in partial fulfillment of University rules and regulations for the award of M.D. degree in Obstetrics and Gynaecology.

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DECLARATION

I, Dr. T. RIZWANA TAJ, solemnly declare that the dissertation titled, "EVALUATION OF EFFICACY OF TRANSDERMAL NITROGLYCERINE IN THE TREATMENT OF PRETERM LABOUR" is a bonafide work done by me at K.A.P.V. Government Medical College, Trichy, during 2008 - 2009 under the guidance and supervision of Prof. Dr. PREMAVATHY PRABHU ELANGO, M.D., DGO., Professor and Head of the department, Obstetrics and Gynaecology. This dissertation is submitted to the Tamilnadu Dr. M.G.R. Medical University, in partial fulfillment of University rules and regulations for the award of M.D. Degree (Branch – II) in Obstetrics and Gynaecology.

Place: Trichy
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CONTENTS

INTRODUCTION

INTRODUCTION

Obstetrics is a fine art built on the facts gathered by scientific research. In the era of modern Obstetrics where there has been a rapid advancement in all specialities, preterm labour remains an enigma for the obstetricians of today.

The social and emotional cost of perinatal mortality and morbidity associated with preterm birth is immeasurable. Ideally preterm labour should be prevented. However pharmacological inhibition of preterm labor remains an effective method to delay preterm delivery and improve neonatal outcome until a most effective means of prevention is identified. Since the Tocolysis has both potential benefits and side effects to neonate and mother, their use should be based on well designed controlled clinical studies.

AIM OF THE STUDY

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Aim of care around preterm birth does not always involve prevention of preterm labour and birth. In situation where clinical condition makes it desirable to prolong pregnancy, primary out come considered is time saved to

- Seek advice from a perinatal care unit
- Institute therapy to improve fetal lung maturity
- If necessary move mother to centre with neonatal intensive care unit

Preterm fetus need glucocorticoids to enhance lung maturity .This can be achieved if delivery is postponed by 24 - 48 hours. Inhibition of uterine contraction at least for 2 days may therefore be regarded as optimal acute tocolysis. A great number of drugs are used to inhibit preterm labour. Aim of our study is to

- Evaluate the effect and safety of transdermal nitroglycerine in acute tocolysis
- Effect of transdermal nitroglycerine on maternal and neonatal outcome

REVIEW OF LITERATURE
DRUG PHARMACOKINETICS

REVIEW OF LITERATURE

DEFINITION

Preterm labour is defined as the onset of regular, painful, frequent, uterine contractions causing progressive effacement and dilatation of cervix occurring before 37 completed weeks of gestation from the first day of last menstrual period.[1] Any infant born before 37 completed weeks should be called as preterm (WHO 1969).

The lower limit which correlates with the fetal viability is less clearly defined. In United States it is 20 weeks. Royal College of Obstetricians and Gynecologist (RCOG) working party considered it as 24 week. In India for legal purposes of viability it is defined as any gestation beyond 28 weeks (196 days).

INCIDENCE

The incidence of pre term labour in developed countries is between 5% to 10%. The incidence in India being 10-14% (FOGSI). In Annal Gandhi Memorial Hospital, Trichy, Incidence of Preterm Labour is 12%.

IMPACT OF PRETERM BIRTH

The most common maternal effects are feeling of inadequacy at fulfilling a reproductive role, more so in women who suffered recurrent pregnancy loss and development of postpartum endometritis.[2]

RISK TO PRETERM INFANT[3]

§ Birth Asphyxia	§ Retrolental fibroplasia
§ RDS	§ Sensorineural deafness
§ Apnea of prematurity	§ Developmental Delay
§ Jaundice	§ Reduced growth potential
§ Hemorrhage	§ Recurrent respiratory infections
§ Metabolic problem	§ Learning difficulties
§ Intraventricular/ Intracerebral hemorrhage	§ Sudden infant death syndrome
§ PDA	§ Cerebral Palsy
§ Necrotizing enterocolitis	§ Enforced separation of mother and baby

It is not uncommon for the smallest surviving infant to incur nursery bills needing several hundred thousand dollars.[4]

ETIOLOGY

Only when the factors causing prematurity are clearly understood, any intelligent attempt at prevention can be made.

Nearly 50-60% preterm births occur following spontaneous labour. 30% is due to preterm rupture of membranes and the rest are iatrogenic.

One of the major reasons for increase in incidence of preterm birth is increase in multiple pregnancies (fertility drugs and artificial reproductive technology) and increased surveillance and intervention in high risk pregnancies

1. Infections [5]

Chorioamnionitis[6] 20-30%

Bobitt and ledger first suggested that unrecognized chorioamnionitis may be casually related to preterm labour. They documented positive cultures during amniotomy via transcervical needle aspiration or intra uterine catheter. The common pathway of intrauterine infection is the ascending route.

Asymptomatic bacterial vaginosis and Trichomonas vaginalis confers a modest risk of spontaneous preterm labour (CDC). Bacterial vaginosis has association with low birth weight.

High prematurity rate is associated with Asymptomatic bacteriuria.

Colonisation of genital tract with group B streptococcus[7] infection is associated with preterm labor.

Colonisation with Chlamydia trachomatis (Martin *et al.*,[8] Harrison *et al.*, 14) Mycoplasma hominis (Klein *et al.*,[9] Harrison *et al.*,) and Ureaplasma Urealyticum[10] are associated with preterm labour.

Edward *et al.*,[11] reported higher incidence of positive gonorrhoea culture in preterm labour.

Extrauterine

Systemic illness like pneumonia, pyelonephritis. Periodontal disease is associated with preterm labour.

2. Placental

- Anatomical abnormalities
- Placenta praevia
- Abruptio placenta

3. Uterine

- Congenital abnormalities 1-3%
- Incompetent Cervix
- Over distention

4. Genetic (Genes for Decidual Relaxin /Fetal mitochondrial Trifuntional protein defect, IL-1, β2 adrenergic receptor gene, tumor necrosis factor –α are implicated).

5. **Vaginal bleeding** in early pregnancy is associated with preterm labour.

6. Fetal

Congenital Anomalies

7. Preterm Labour of unknown origin 20-30%

PATHOPHYSIOLOGY

The control of parturition is achieved by complex integration of endocrine, paracrine and autocrine mechanism.

1. The fetal pituitary adrenal axis needs to be intact.
2. The role of oxytocin and oxytocin – prostaglandin interaction is still unclear (Fuch's *et al.*, 1984).[12]

Cox and colleagues[13] (1993) found that cytokines (1LI, 1L6, TNFα, IL8) are released when there is inflammatory response to infection and intrauterine bleeding. These inturn stimulate arachidonic acid and prostaglandin production.

Differential production of PGE_2 and PGF_2 by the three enzymes – phospholipases, PGH_2 synthase, 15 hydroxy prostaglandin dehydrogenase may be a key in the balance between uterine quiescence and activity. This decidual activation and production of uterotropins is the penultimate event in initiation of labour.[14]

EPIDEMIOLOGY

1. Race[15]

The incidence is greater among black women.

2. Age

It is more common in extremes of age. Lumley *et al.,* 1993 reported high incidence of preterm delivery in women under 20 years and over 35 years.

3. Weight

Poor nutrition, prepregnancy weight and weight gain during pregnancy play an important role in causing preterm birth. Hickey and colleagues 1995, have shown low maternal prenatal weight gain is specifically associated with preterm birth.

4. Stature

Short statured mothers have more tendency to produce smaller babies.

5. Socio-Economic Status

Women from lower socio economic status tends to be less educated and would not have satisfactory general or antenatal care and hence more incidence of preterm labour.

6. Addictions

Women who smoke cigarettes or who abuse cocaine are at increased risk of preterm labour (Bakketing and Hoffman, 1981).[16]

7. Occupational Factors

Those involved in manual work are more prone for preterm labour.

PREDISPOSING FACTORS

1. Stress

Careers which involve physical fatigue and high psychological stress are associated with increased incidence of preterm labour.[17] Prolonged standing decreases uteroplacental blood flow and increases the frequency of uteroplacental insufficiency causing growth retardation. Preterm birth is increased in women living alone, and in those who are subjected to physical abuse.

2. Coitus[18]

Coitus was not found to be associated but increasing numbers of sexual partners increased the risk of recurrent preterm delivery.

3. Reproductive History

a. Previous preterm Birth

The history of one previous preterm birth is associated with recurrent risk of 16-41% and the risk increases with the number of preterm birth and decreases with the number of term deliveries.[19]

b. Previous abortion

There is an increase in the incidence of preterm deliveries in women who experience one or more second trimester abortions.

c. Cervical incompetence

d. Uterine anomalies

4. Pregnancy complications

- Multiple pregnancies
- Hydramnios
- Preclampsia
- Antepartum hemorrhage
- Second trimester bleeding not due to placental causes

5. Interpregnancy interval[20]

A significant increase in preterm birth was observed when the interval between previous child birth and LMP of next pregnancy was less than 3 months.

6. Fetal Gender

The main fetal factor influencing the rate of preterm delivery is fetal sex in the preponderance of males delivering preterm.

RISK SCORING SYSTEM

A risk scoring system devised by Papiernik and modified by Creasy and Govik[21] (1986) has been tested in several regions. Women with scores of 10 or more are considered to be at high risk for preterm labour.

Scoring systems is based on the factors which increase the risk of preterm delivery, the risk is highest with a previous preterm delivery. Bleeding in pregnancy, Urinary tract infections, higher order pregnancies, body mass index < 20kg /m^2, previous low birth weight babies and stress (family illness, mortality, violence, financial) are associated with preterm delivery. Unfortunately risk scores don't identify the majority of women who deliver preterm. They are of limited clinical use.

PAPIERNIK RISK SCORING SYSTEM

Points	Socio-economic factors	Previous Medical History	Daily Habits	Aspects of Current Pregnancy
1	Two children at home, Low socio-economic status	Abortion × 1, less than 1 yr since last birth	Works outside	Unusual Fatigue
2	Maternal age < 20 yrs or > 40yr, Single parent	Abortion × 2	Smokes more than10cigarettes per day, more than 3 flights of stairs without elevator	Gain of <5Kg by 32 weeks
3	Very low socio-economic status Height <150cm Weight<45 kg	Abortion × 3	Heavy or stressful work that is long and tiring, Extensive traveling, long daily commuting	Breech at 32 wks Weight loss, Head engaged at 32 wks, Febrile illness.
4	Maternal age < 18 yrs	Pyelonephritis		Bleeding after 12 weeks, Short Cervix, Opened internal OS, Uterine irritability.
5		Uterine anomaly, Second trimester abortion, DES exposure, cone biopsy		Placenta previa, Hydramnios
10		Preterm delivery, Repeated second trimester abortion		Twins, Abdominal surgical procedure

PREDICTION OF PRETERM LABOUR

1. CERVICAL ASSESSMENT

Asymptomatic cervical dilatation after mid pregnancy has gained attention as a risk factor for preterm delivery. Leveno[22] and associates found that one fourth of the women whose cervices were dilated 2 to 3 cm between 26 and 30 weeks delivered before 34 weeks. By routine cervical examination the sensitivity of predicting preterm labour is 63% in nullipara and 53% in multipara.

2. UTERINE ACTIVITY MONITORING

Katz[23] and associates found that women who had subsequent preterm delivery had increased uterine contraction at 30 weeks.

Home uterine contraction monitoring was investigated by many and found to be successful. Currently ACOG (1995) has not clearly demonstrated the usefulness of this expensive and burdensome system in preventing preterm labour.

3. FIBRONECTIN

The presence of fetal fibronectin in cervicovaginal secretions has to be proposed as a specific predictor of preterm labour. (Lockwood and Coworkers, 1991).[24] It can be measured using ELISA and values exceeding 50mg/ml are considered positive result. However of most

concern is the high false positive rate with microscopic contamination with amniotic fluid or semen, maternal blood and in patients with cerclage. The test is more accurate in predicting spontaneous preterm birth within 7-10 days in women with symptoms of threatened preterm labour before advanced cervical dilatation.

The high negative predictive value of fetal fibronectin can be used to influence management.

4. USG

Honest *et al.*,[25] found that in asymptomatic women ultrasonography measurement of cervical length using cut off of 25 mm or less between 20-24 weeks gestation is likely to be accurate in predicting spontaneous preterm birth.

BIOCHEMICAL MARKERS

1. Salivary oestriol : Progesterone ratio
2. Serum Collagenase
3. Tissue inhibitor of metalloproteinase (TIMP)
4. Relaxin
5. Corticotrophin releasing hormone (CRH)
6. Mediators of inflammation and infection.

a. CRP[26]
b. Leucocyte esterase
c. Cytokines[27]
d. Amniotic fluid glucose concentration
e. Zinc
f. Lipocortin – 1
g. Positive cultures

These are not practically helpful in prediction of preterm labour.

DIAGNOSIS OF PRETERM LABOUR

1. Symptoms of preterm labour[28]

- Menstrual like cramps
- Low, dull back ache
- Abdominal cramping
- Change in vaginal discharge
- Uterine contractions that are 10 minutes apart or closer

Cunningham GH and coworkers (2001) found that preterm labour is considered to be established if regular uterine contractions can be documented at least 4 in 20 minutes or 8 in 60 minutes with progressive change in cervical score with effacement 80% or more and dilatation more than 1 cm.

If there is absence of cervical change in the presence of contractions the condition is Threatened Preterm Labour.

2. Pelvic examinations

3. Ultrasonogram

Ultrasonogram assessment in preterm labour.

- Fetal viability
- Gestational age
- Estimated fetal weight
- Indicators of preterm labor – Cervical Length and width of internal os
- Amniotic fluid volume
- Number of fetus
- Fetal presentation and lie
- Fetal movement and tone
- Fetal gender
- Fetal anomaly
- Placental localisation and morphology
- Uterine fibroid

4. Toco Cardiography

The amplitude, duration, frequency of contraction, and basal tone are monitored. The uterine activity is expressed in Montevideo units.

PREVENTION OF PRETERM LABOUR

1. Basic Care

- Support system of family and friends should be developed
- Numerous suggestions on coping with physical and mental stresses of maintaining a pregnancy should be described
- Education, supportive services from health care providers and financial issues are also of common concern.
- Behavioural and lifestyle modification
    a. Smoking cessation
    b. Avoidance of illicit drugs
    c. Adequate nutrition

2. Bed rest and Hydration

Although bed rest and hydration are widely used as the first step of prevention and treatment, there is no evidence that this practice is beneficial.

Bed rest should be advised with caution after evaluating its benefits and risks in an individual, and not routinely keeping in mind its adverse effects like venous thrombosis and pulmonary edema.

3. Aggressive treatment of cervicovaginal infection

Bacterial vaginosis has been consistently associated with a 1.5 to 3 times increased risk of spontaneous preterm birth. But the efficacy of treatment in reduction of preterm birth is conflicting. But recent systematic review showed that screening and treatment of asymptomatic bacteruria and bacterial Vaginosis in low risk population may reduce the rate of preterm deliveries.

4. Cervical Encerclage

A short cervix diagnosed by ultrasound in asymptomatic women may be an indication for cerclage. The role of cervical cerclage for the prevention of preterm delivery is now disputed as cerclage has a inherent risk which actually increase preterm labour by increasing the pericervical inflammation or infection.

5. Progesterone

Weekly intramuscular administration to women at high risk for preterm labour resulted in lower rates of preterm birth and perinatal

mortality when compared to placebo. The dose used was 250 mg of 17-hydroxy progesterone caproate intramuscularly every week from 20 to 36 weeks.

MANAGEMENT OF PRETERM LABOUR[29]

a. Bed rest and hydration

b. Steroids

In 1994, a National Institute of Health Consensus Development Panel recommended corticosteroids for fetal lung maturation in preterm labour.[30] Since then, there has been nearly universal acceptance and implementation of these recommendations.

All pregnant women between 24 and 34 weeks of gestation who are at risk of preterm delivery within 7 days should be considered candidates for antenatal corticosteroids.

Recommended regimens includes a single course of two doses of 12 mg of betamethasone given intramuscularly 24 hours apart, or four doses of 6mg of dexamethasone given intramuscularly 12 hours apart.

A Cochrane Systematic Review found that antenatal corticosteroids reduce neonatal death, respiratory distress syndrome, intraventricular hemorrhage. Also antenatal corticosteroid is not associated with changes in the rates of maternal death, maternal infection, fetal death, neonatal

chronic lung disease or birth weight. It is also associated with a reduction in incidence of neonatal enterocolitis and systemic infections in the first 48 hours of life as well as reduction in the need for respiratory support or neonatal intensive care unit admission.

Although benefit on neonatal outcome is maximum between 24 hours and 7 days after initiation of therapy, steroids confer significant survival advantages even when delivery occurs within 24 hours. Therefore treatment should not be withheld when delivery is probable within 24 hours.

c. Tocolysis - In early preterm labour to provide time for steroids to act

Tocolysis is pharmacological suppression of unwanted uterine activity.

Criteria for tocolytic therapy

- Gestational age between 20 and 34 weeks from LMP
- Expected fetal weight less than 2kg by ultrasonography
- Membranes intact
- Cervical dilatation less than 3 cm.
- Alive uncompromised fetus
- Regular uterine contraction with progressive cervical changes.

TOCOLYTICS IN PRETERM LABOUR[31]

1. PROGESTOGENS

Fuch and Stakeman (1960), Brenner and Hendricks (1962), Olivesen and Hell *et al.* (1975) have investigated the use of progestogens and were unable to show any inhibitory effect on uterine contraction. Johnson *et al.*[32] (1975) found that 17 αOH progesterone caproate was able to prevent preterm labour. Two recent metaanalysis indicate that progestogenic agents reduce the occurrence of preterm birth.

2. ETHANOL[33]

Fuch *et al.* (1967) the principal advocate of this mode of therapy gave a loading dose of ethanol followed by maintenance dose for further 10 hours. The over all success rate was 65%. Complications include nausea, vomiting, headache and restlessness. They act centrally by decreasing the amount of oxytocin.

3. BETA SYMPATHOMIMETICS

Rucker in 1925 noted that small doses of epinephrine inhibited uterine hyperactivity. Efforts to produce an epinephrine like compound which lacked the cardiovascular stimulant effect culminated in the synthesis of β agonists.

I generation : Isoxsuprine, orciprenaline, Isoprenaline

II generation: Ritodrine,[34] Terbutaline,[35] Fenoterol.

Unfortunately in terms of clinical effectiveness the inhibition of contractions by β adrenergic agonists is often short lived.

Maternal side effects

- Tachycardia
- Hypotension
- Cardiac arrhythmias
- Myocardial ischaemia
- Pulmonary edema

Contraindications

- Symptomatic cardiac disease especially ventricular outflow obstruction
- Conduction disturbance
- Hyperthyroidism
- Sickle cell disease
- Uncontrolled IDDM
- Chorioamnionitis
- Eclampsia or severe preeclampsia

- Multifetal gestation
- Severe obstetrical bleeding
- Severe Anaemia
- Patients on MAO inhibitors
- Asthmatic patients already on β adrenergic agents.

MAGNESIUM SULPHATE

$MgSO_4$ uncouples the depolarization contraction coupling (Elliott, 1983).[36] Most commonly used for the prevention and treatment of seizure in preeclampsia but its tocolytic effect recognized since 1959. Therapeutic level for both indications is 4-8 m mol per litre. Increased concentration than this leads to neuromuscular blockade, respiratory depression, cardiac arrest. It crosses placenta and new born baby may be drowsy.

PROSTAGLANDIN SYNTHETASE INHIBITORS

Drugs like aspirin, indomethacin[37] are used as an alternative to β agonist to prevent preterm labour in patients with cardiac disease and hyperthyroidism. Not routinely used because of fear of PDA closure and pulmonary hypertension in fetus.

CALCIUM CHANNEL BLOCKERS[38]

They are heterogenous group of organic compounds that inhibit the influx of extracellular calcium across the cell membrane during inward calcium current of action potential. They also inhibit the release of intracellular calcium from the sarcoplasmic reticulum. Thus they reduce the tone of smooth muscles.

The commonly used drug Nifedipine is a potent inhibitor of myometrial contractions in non pregnant, pregnant and post partum uterus.

Side effects

- Dizziness
- Flushing
- Headache
- Peripheral Edema
- Fetal hypoxia

OXYTOCIN ANTAGONIST (ATOSIBAN)[39]

There will be increase in myometrial oxytocin receptors in labour. This analogue competitively blocks the oxytocin receptors and inhibits preterm labour. RCOG guidelines suggest that if tocolytics are

administered, the first choice should be oxytocin antagonists or Nifedipine. But compared with other tocolytics atosiban therapy is costly.

NITRIC OXIDE DONORS (GLYCERYL TRINITRATE)[40]

The Nitric Oxide donors inhibit corticotrophin releasing hormone secretion which acts as a promoter of parturition. This was listed at Kings College Hospital (Lees *et al.*, 1994).[41]

Nitric Oxide is an endogenously occurring biatomic molecule and can be given in the form of nitric oxide donor. First recorded use of nitric oxide donor in pregnancy was reported in British journal 1882 when amyl nitrite was used to deliver morbidly adherent placenta. Nitroglycerine used intravenously as uterine relaxant to aid breech extraction. Breech extraction was facilitated by Nitroglycerine spray (Lancet 1991). Nitroglycerine spray was also used to assist in replacing an inverted uterus in case of retained placenta.

Nitric Oxide donors causes smooth muscle relaxation and effect on uterine muscle is more pronounced during pregnancy than delivery.

POTASSIUM CHANNEL OPENERS

These newer group of drugs which hyperpolarize excitable tissues and function as potent smooth muscle relaxant. Maximum inhibition is

achieved at micromolar concentration. The outward current of potassium offsets depolarizing stimuli and so suppress the regenerative electrical activity thereby rendering the myometrial cell quiescent. Further evaluation is needed.

DRUG PHARMACOKINETICS

NITROGLYCERINE PATCH

Recent reports indicate that nitric oxide released from L-arginine is central to inhibit uterine activity during gestation. Taking this fact into consideration, it was thought that perinatal salvage can be dramatically improved by using transdermal nitroglycerine as a tocolytic agent.

MECHANISM OF ACTION

Organic nitrates are rapidly denitrated enzymatically in smooth muscle cell to release nitric oxide which activates Guanyl cyclase thereby increasing CGMP which causes dephosphorylation of myosin light chain kinase (MLCK). Reduced availability of phosphorylated MLCK interfere with activation of myosin. It fails to interact with actin to cause contraction. Consequently relaxation occurs. Raised intracellular CGMP may also reduce calcium entry contributing to relaxation.

ROLE OF NITRIC OXIDE IN PREGNANCY

Nitric oxide is basically responsible for relaxation of smooth muscle in myometrium. The myometrial concentration of nitric oxide increases significantly in early pregnancy. But in late pregnancy, there is a decrease in nitric oxide level in myometrium and decidua. Therefore

contractile status increases towards term. Conrad et al localized nitric oxide in syncytio trophoblast of human placenta.

Recently it has been established that Nitric oxide as EDRF plays a very important role in uteroplacental circulation. It decreases both resistance and pulsatility index in both umbilical and uterine arteries and thereby increases uteroplacental blood flow.

COMPOSITION

Transdermal (TTS) containing 25 mg (TTS-5), 50 mg (TTS-10) and 75 mg (TTS-15) are available for use.

PROPERTIES

TTS is a flat multi layered patch designed to deliver nitroglycerine continuously through a release membrane. TTS-10 denotes normal amount of Nitroglycerine in mg delivered by system / 24 hours. When Nitroglycerine content is 50 mg, rate of drug release / hour is 0.4 mg.

ABSORPTION

Following single application, placental concentration of Nitroglycerine reaches a plateau at 2 hours and is maintained for 24 hours. It has bioavailability of 70-90%.

DISTRIBUTION

Same plasma levels are obtained regardless of site of application of patch and distribution of drug is equal.

METABOLISM

Transdermal Nitroglycerine is rapidly metabolized by glutathione dependent organic nitrate reductase in liver and excreted in urine.

ELIMINATION

Plasma concentration drops below the level of detection within 1 hour of removal.

MATERIALS AND METHODS

MATERIALS AND METHODS

STUDY DESIGN

It is a prospective randomized controlled trial. The study was conducted in Annal Gandhi Memorial Hospital, Trichy from August 2008 to July 2009. 100 patients with preterm labour randomly selected from patients attending antenatal OPD and from labour ward. 50 patients recruited for nitroglycerine patch and another 50 patients for bed rest alone. Both the groups received intramuscular corticosteroids. In view of the ethical issue, written informed consent was obtained.

INCLUSION CRITERIA

1. Gestational age between 28 to 34 wks as determined by menstrual dates, clinical examination, USG.
2. Uterine contractions: 2 contractions in 10 minute period, each contraction lasting for 40 sec.
3. Progressive cervical effacement upto 75%.
4. Cervical dilatation upto 3 cm.
5. Intact membranes.

EXCLUSION CRITERIA

Maternal Factors

1. Rupture of Membrane
2. Infection
3. Cervical dilatation greater than 3 cm
4. Antepartum hemorrhage
5. Pregnancy induced hypertension
6. Chronic hypertension
7. Cardiac disease
8. Previous caesarean section
9. Renal disease
10. Pulmonary disorder – Asthmatics, ARDS.

Fetal Factors

1. Multiple gestation
2. Fetal death / distress
3. IUGR
4. Congenital anomalies
5. Polyhydramnios / Oligohydramnios
6. Erythroblastosis

Investigations

1. Urine analysis
2. Complete Blood count
3. Vaginal swab
4. USG

DRUG PROTOCOL

On admission, patients were put in left lateral position. BP, pulse rate recorded. CVS, RS examined.

GROUP A

5 mg of Nitroglycerine patch applied to the skin of the abdomen. Even after 1 hour, if there was no decrease in the frequency and strength of uterine contractions, an additional patches were applied. Maximum dose is 20 mg in 24 hours. Patches were removed after 24 hours and same number of fresh patches were applied for the next 24 hours.

Treatment discontinued if

- BP falls < 90 / 60 mm Hg
- PR > 100 / min
- Patient had PROM

- Uterine contractions persist for > 24 hours even after applying 20 mg of Nitroglycerine patch.

GROUP B

Observed with bed rest.

Common for Group A & B

2 doses of Betamethasone[42] 12 mg IM 24 hours apart is given.

Monitoring

Maternal	Fetal
Pulse Rate	Heart Rate
Blood Pressure	Rhythm
Uterine contractions	Tone

All were monitored every 30 mins for 1st 2 hours. Then every 2 hours for 12 hours. Then 4 hourly for 48 hours.

Side effects of Nitroglycerine Patch

- Headache
- Tachycardia
- Hypotension
- Dizziness

- Weakness
- Skin irritation

Definition of Success

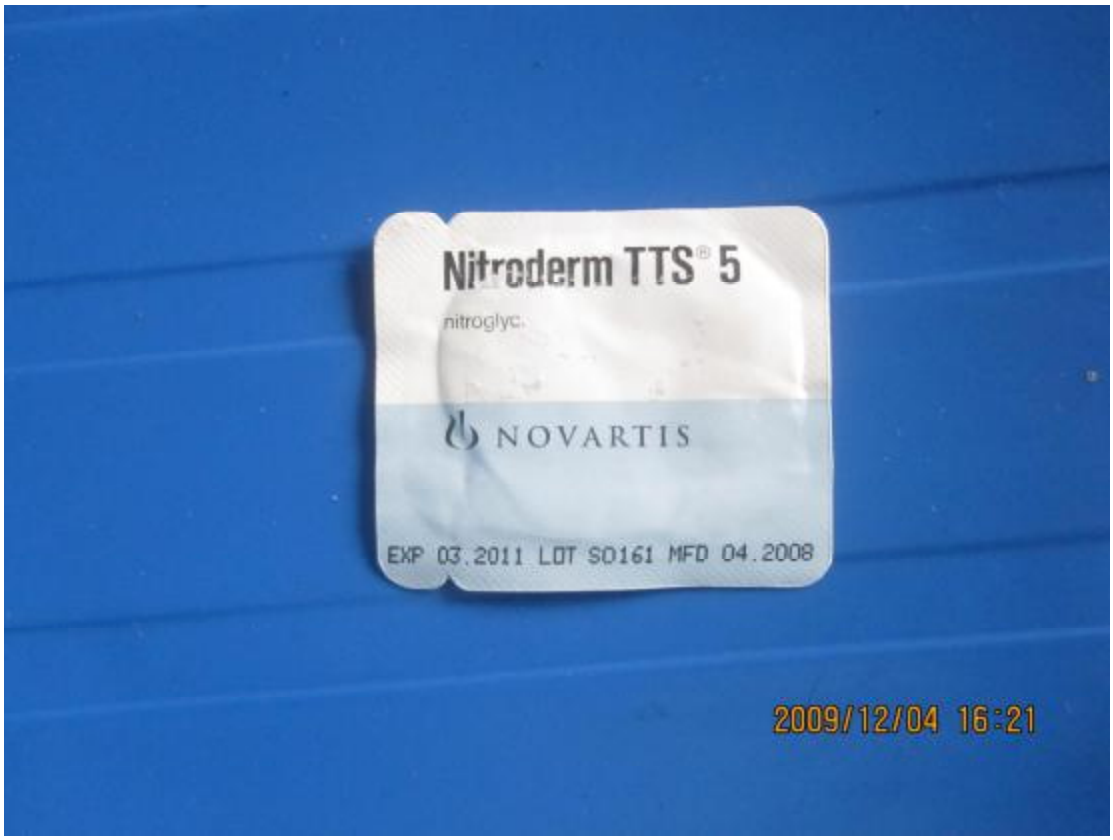
Treatment is considered successful if uterine contraction subsided and tocolysis achieved for > 48 hours.

Definition of failure

The therapy was said to have failed when the patient delivered within 48 hours of initiation of therapy. Tocolytic was stopped when cervical dilation progressed to > 3 cms or when the membranes ruptured spontaneously.

Hence this study confines itself to the study of idiopathic spontaneous preterm labour, comparing the efficacy of nitroglycerine patch with that of control group in prolonging pregnancy for atleast 48 hours and studying the maternal and fetal effects.

NITROGLYCERIN PATCH



ANALYSIS OF RESULTS

ANALYSIS OF RESULTS

Study was designed with total sample of randomly selected 100 cases who were in Preterm labour, out of which 50 females were randomly allotted for Nitroglycerine patch in group A and another 50 patients in group B observed with bed rest alone. All patients on study were given corticosteroids. Prophylactic antibiotics also were given to all patients. After inspection of pooled outcome data, the following results were observed.

AGE DISTRIBUTION

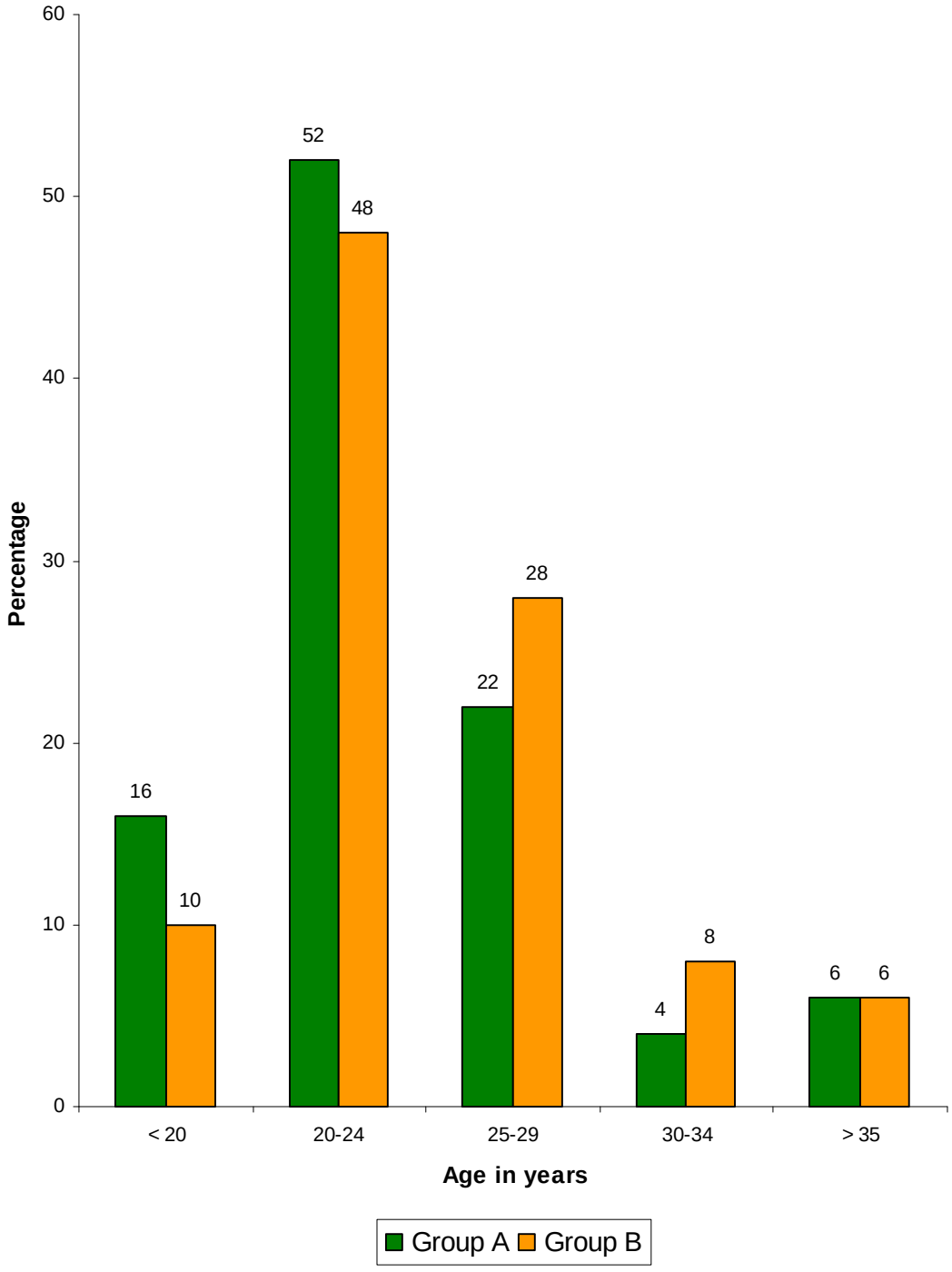
Table - 1

Age in Years	Group A		Group		Total
	No.	%	No.	%	
< 20	8	16	5	10	13
20-24	26	52	24	48	50
25-29	11	22	14	28	25
30-34	2	4	4	8	6
>35	3	6	3	6	6
Total	***50***	***100***	***50***	***100***	***100***

P value = 0.764

Age distribution of 2 groups of patients had no much significant difference. P value - 0.764 (> 0.05). Majority of patients in both the groups fall in the age group 20-24 yrs. The mean age group of study subjects was 23.9 years.

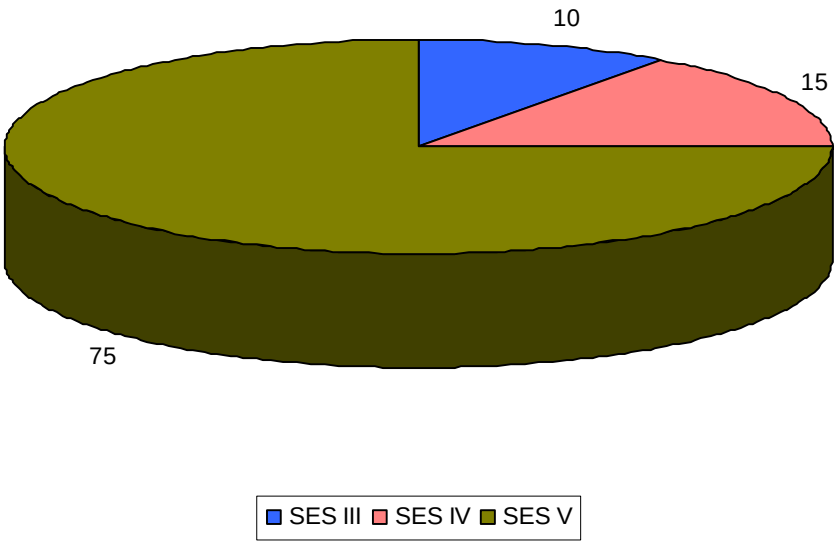
AGE DISTRIBUTION



SOCIOECONOMIC STATUS

Patients from SES V constituted 75%, SES IV 15%, SES III 10%. Preterm labour is common in low socio economic and nutritional status.

SOCIO-ECONOMIC STATUS



ANTENATAL CARE

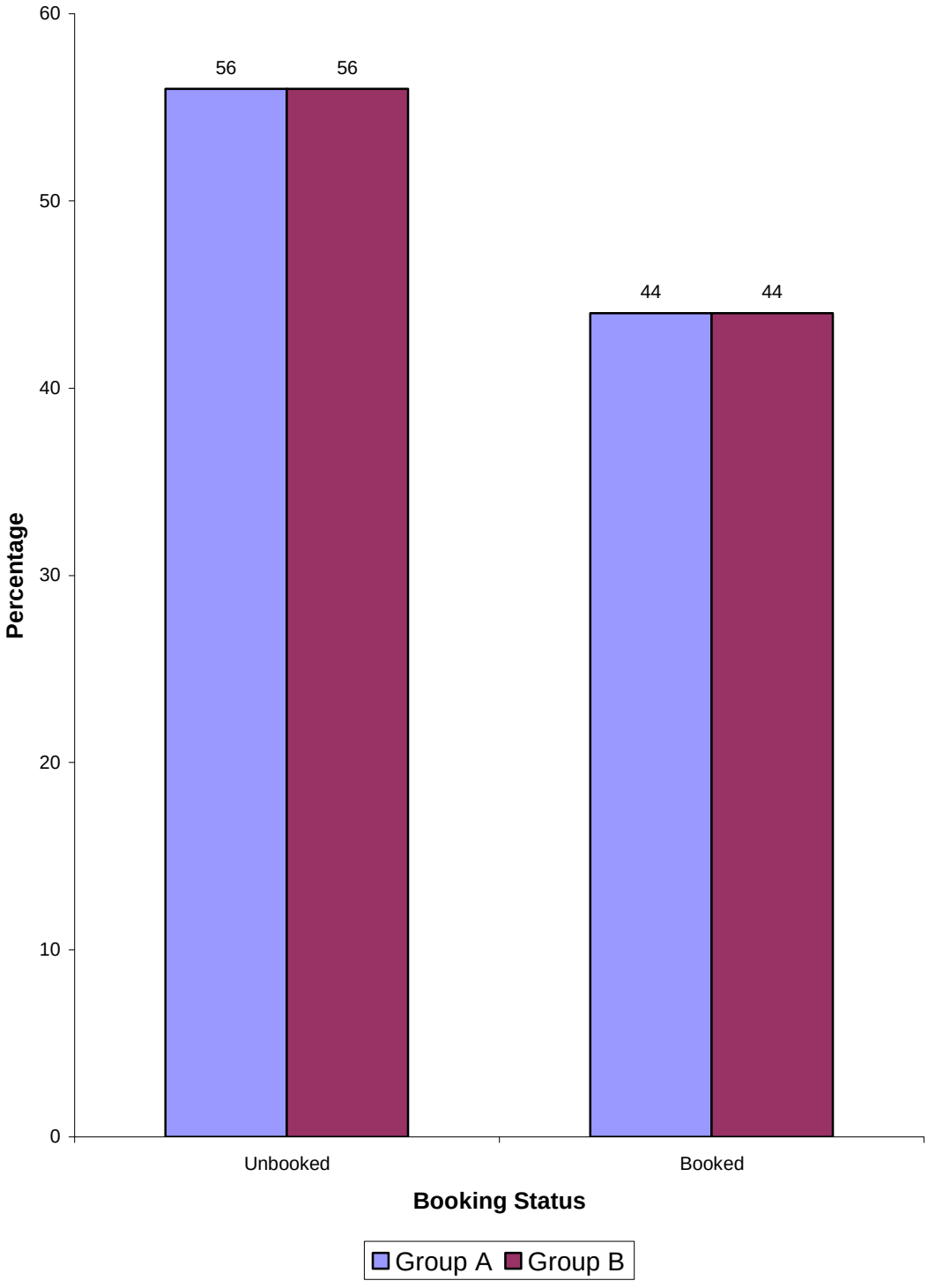
Table - 2

S. No.	ANcare	Group A		Group B	
		No.	%	No.	%
1.	Unbooked	28	56	28	56
2.	Booked	22	44	22	44

P value = 0.5

Preterm labour was more common among unbooked patients while the booked patients who had atleast 3 visits were educated about preterm labour and complications. Regular antenatal care was received by 44% of patients in both Group A & B.

ANTENATALCARE



PARITY

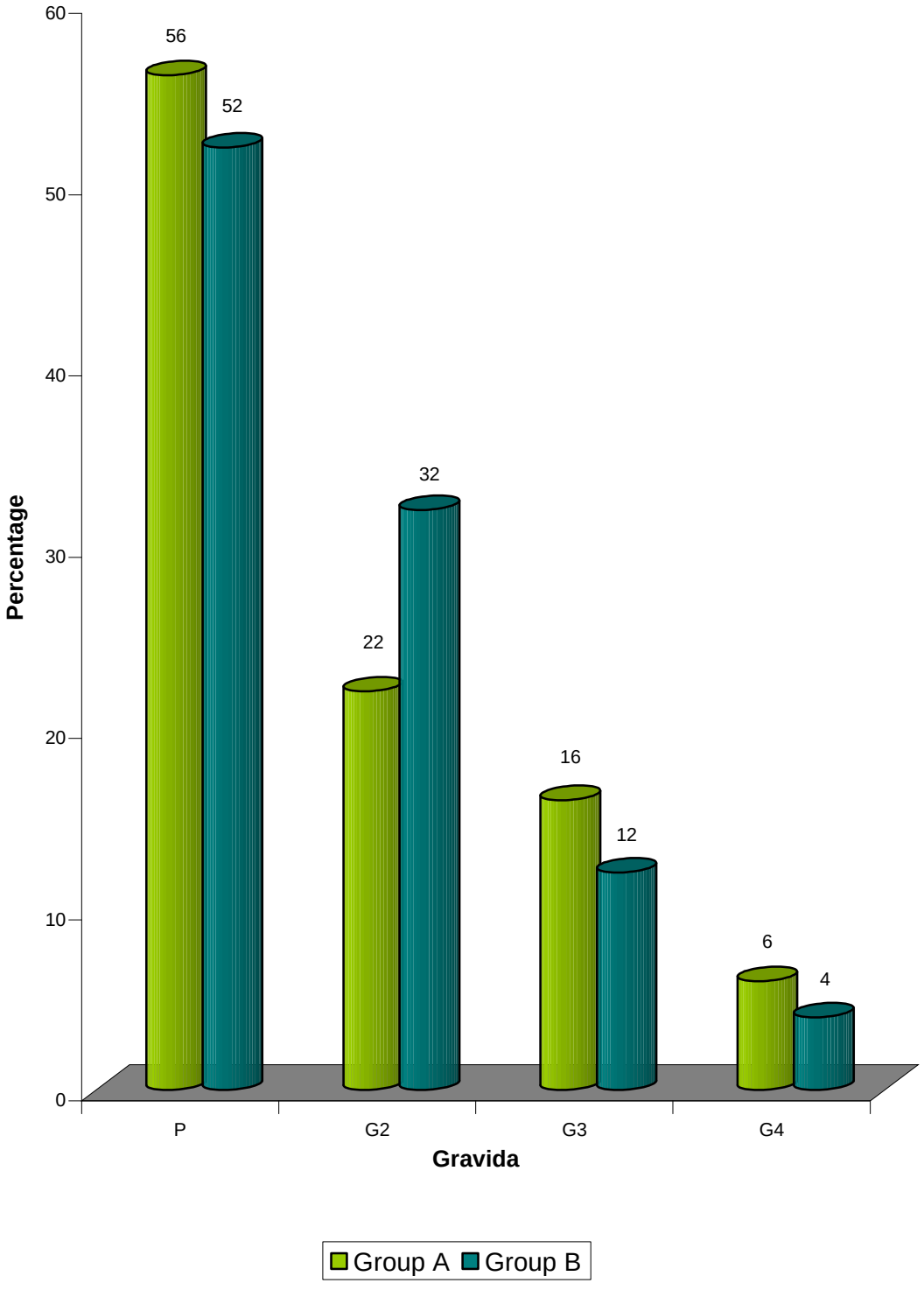
Table - 3

S. No.	Gravida	Group A		Group B	
		No.	**%**	**No.**	**%**
1	P	28	56	26	52
2	G2	11	22	16	32
3	G3	08	16	06	12
4	G4	03	06	02	04
	Total	***50***	***100***	***50***	***100***

P value = 0.686

Parity selection did not have much significant difference in both groups (P > 0.05) Primi 56% in Group A and 52% in Group B. Multi- 44% in Group A and 48% in Group B.

PARITY


60
50
40
30
20
10
0
Percentage
56
52
22
32
16
12
6
4
P
G2
G3
G4
Gravida
Group A
Group B

PREVIOUS HISTORY OF PRETERM LABOUR

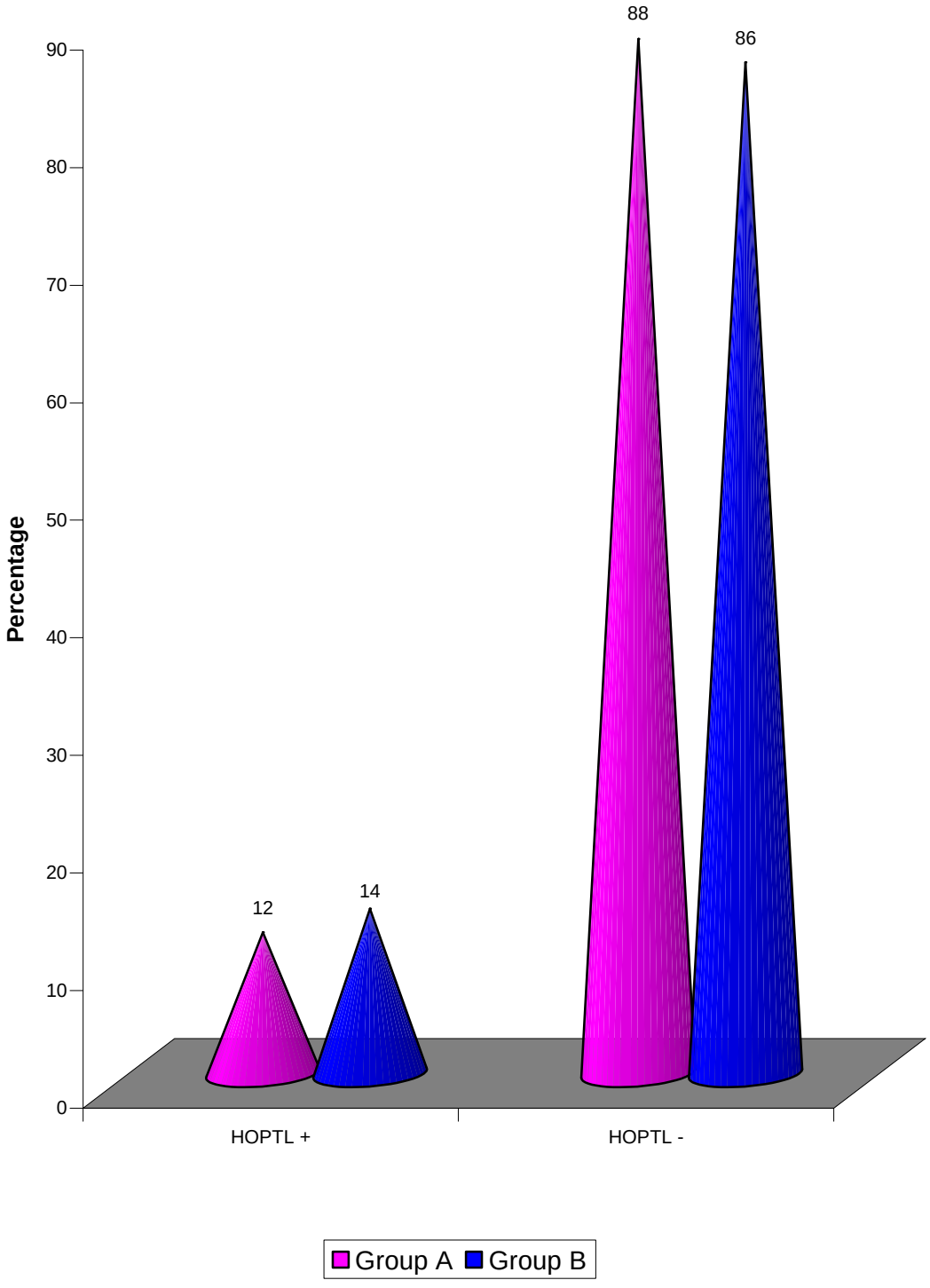
Table - 4

S. No.	H/O PTL	Group A		Group B	
		No.	%	No.	%
1.	Yes	6	12%	7	14%
2.	No	44	88%	43	86%

P value = 0.5

There was no significant difference in history of Preterm labour between 2 groups of patients. Majority of patients selected for this study experienced preterm labour for the first time.

PREVIOUS HISTORY OF PRETERM LABOUR



PRESENTATION

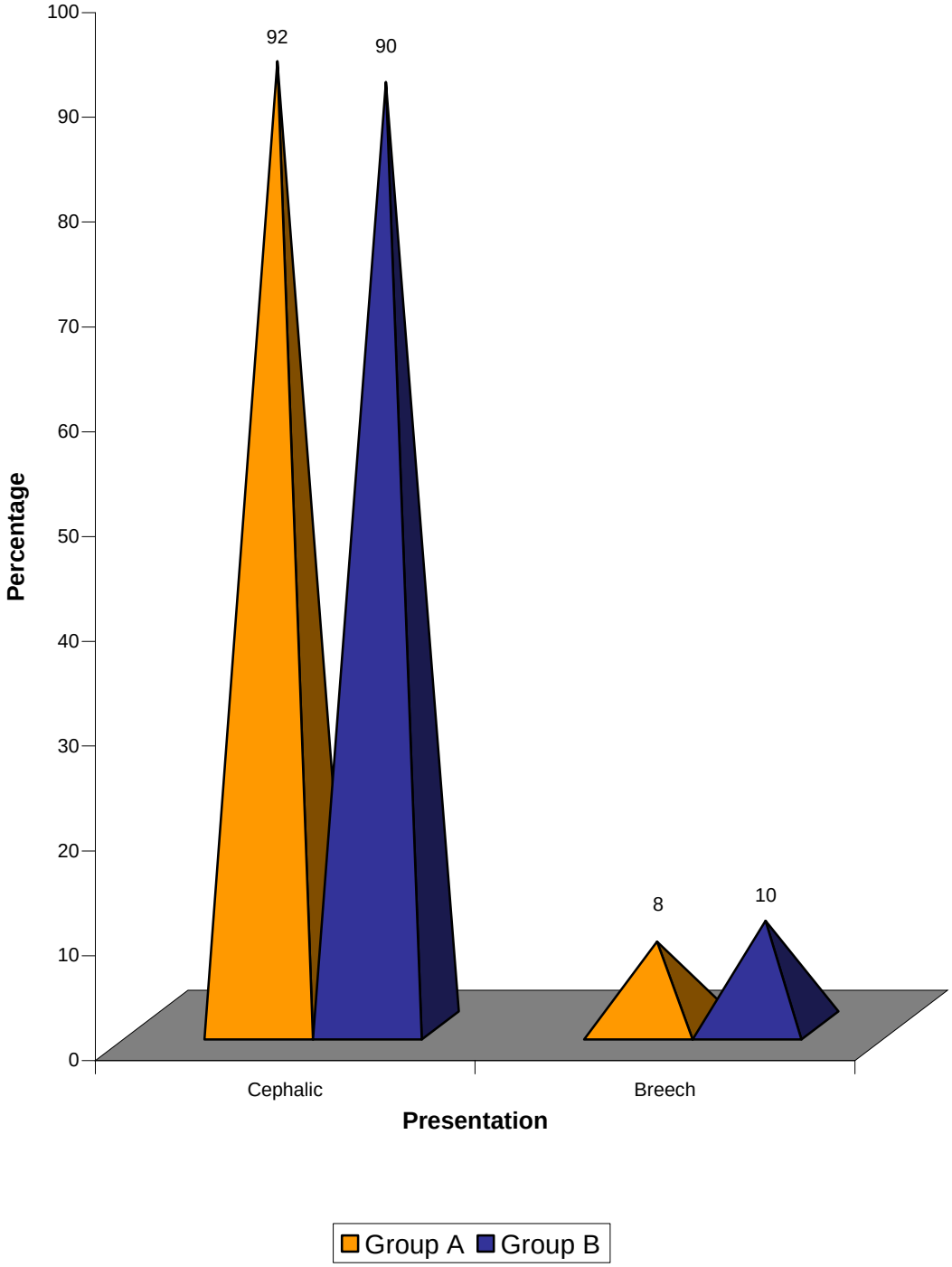
Table - 5

S. No.	Presentation	Group A		Group B	
		No.	%	No.	%
1.	Cephalic	46	92%	45	90%
2.	Breech	4	8%	5	10%

P value = 0.5

Maximum number of patients in both the groups had cephalic presentation.

PRESENTATION



GESTATIONAL AGE

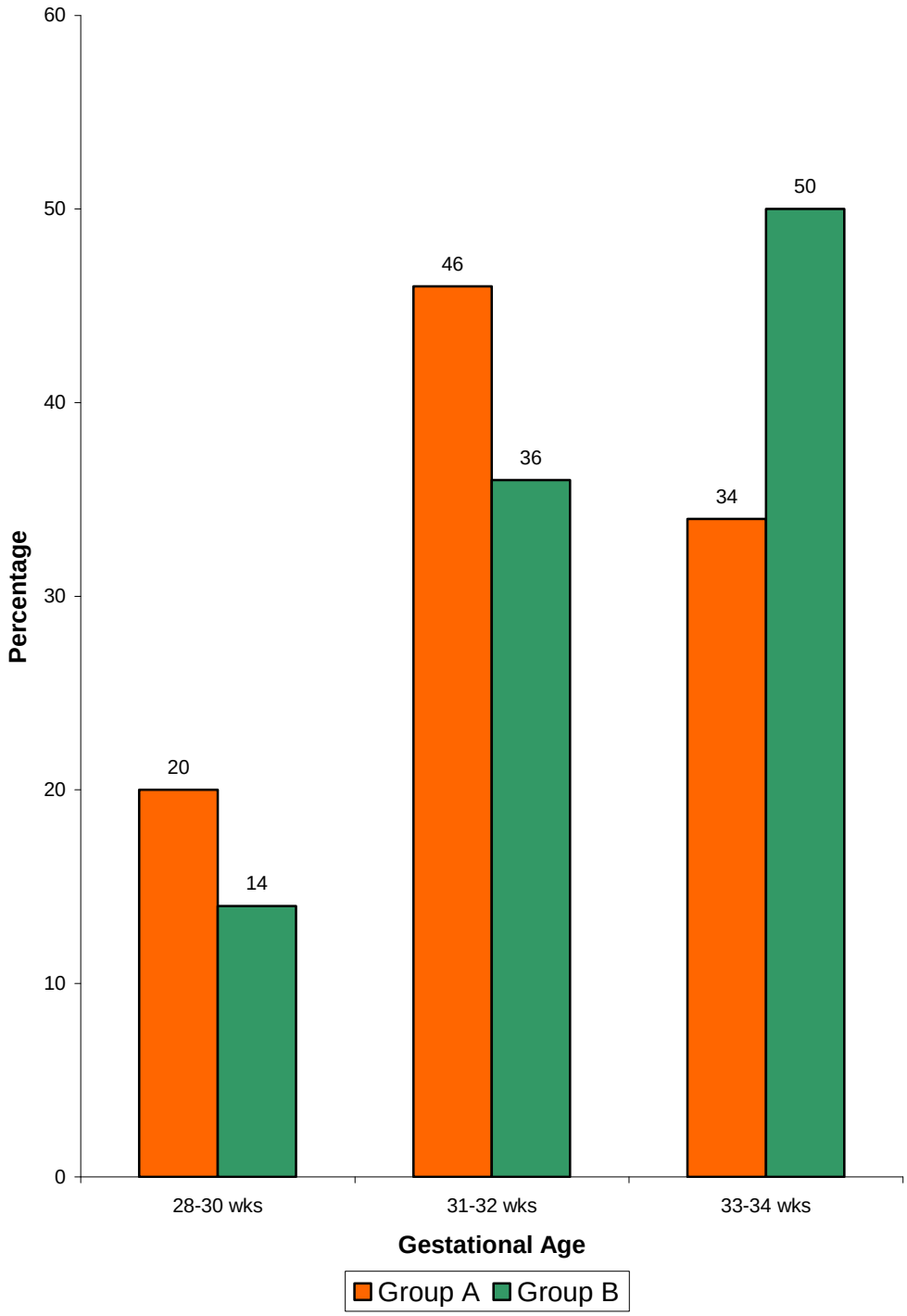
Table - 6

S. No.	Gestational Age	Group A		Group B	
		No.	%	No.	%
1.	28-30 wks	10	20%	7	14%
2.	31-32 wks	23	46%	18	36%
3.	33-34 wks	17	34%	25	50%

P value = 0.058

Time of prolongation of pregnancy varied considerably with Gestational age at entry in both groups. 20% of patients in group A and 14% in group B had gestational age of 28-30 weeks. 46% in group A and 36% in group B belonged to gestational age 31-32weeks. In 33-34 weeks there were 34% of patients in group A and 50% in group B.

GESTATIONAL AGE



DURATION OF PROLONGATION

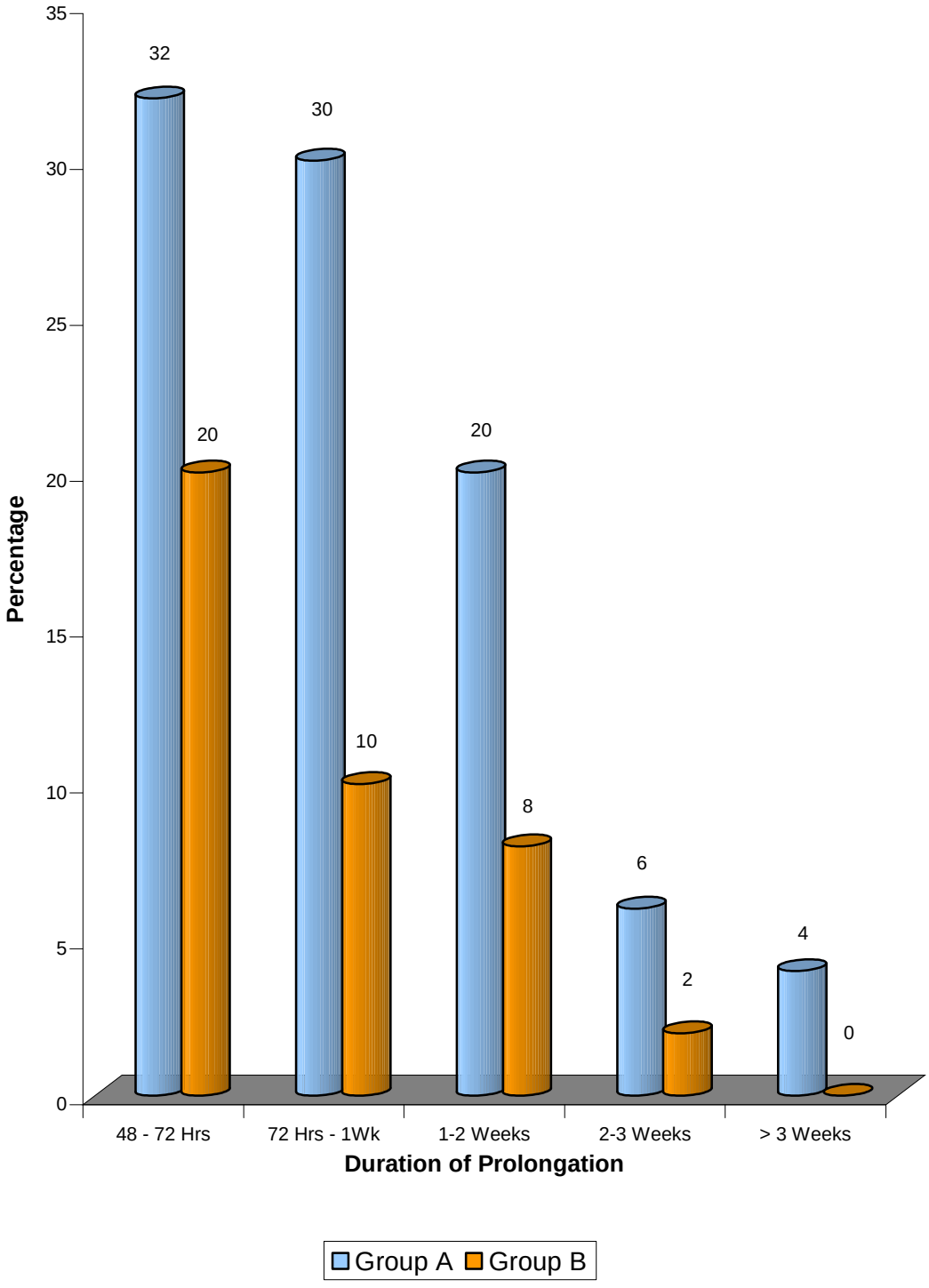
Table - 7

S. No.	Duration	Group A		Group B	
		No.	%	No.	%
1.	48 - 72 hrs	16	32%	10	20%
2.	72 hrs - 1 wk	15	30%	5	10%
3.	1-2 wks	10	20%	4	8%
4.	2-3 wks	3	6%	1	2%
5.	>3 wks	2	4%	0	0

P value = 0.014

Prolongation beyond 1 week was observed in 30% in group A and 10% in group B. Mean duration of prolongation of pregnancy in Group A was 6.6 days.

DURATION OF PROLONGATION



RESPONSE ACCORDING TO GESTATIONAL AGE

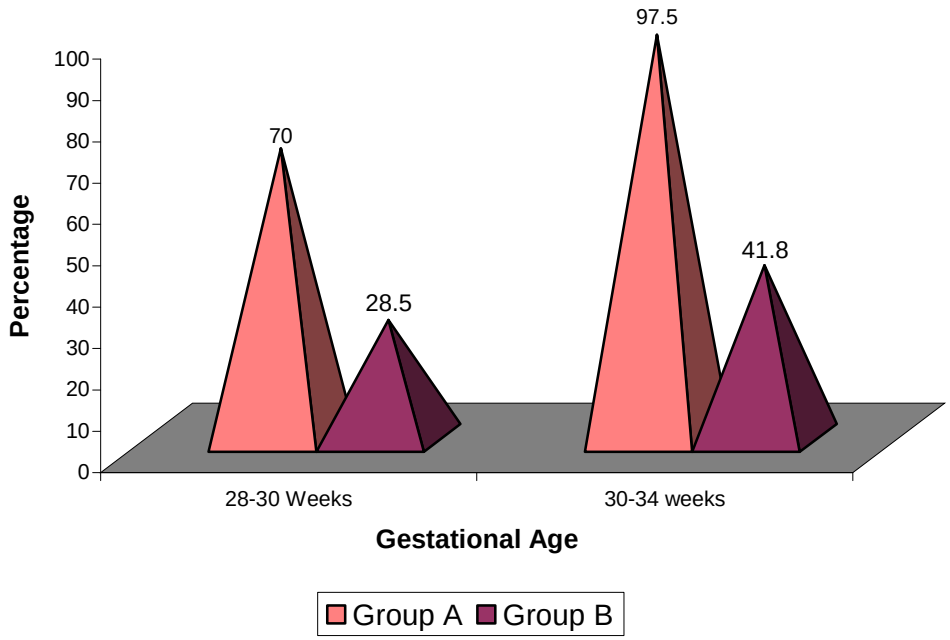
Table – 8

S. No.	Gestational Age	Group A		Group B	
		Success	Failure	Success	Failure
1.	28-30wks	7(70%)	3(30%)	2(28.5%)	5(71.5%)
2.	30-34wks	39(97.5%)	1(2.5%)	18(41.8%)	25(58.1%)

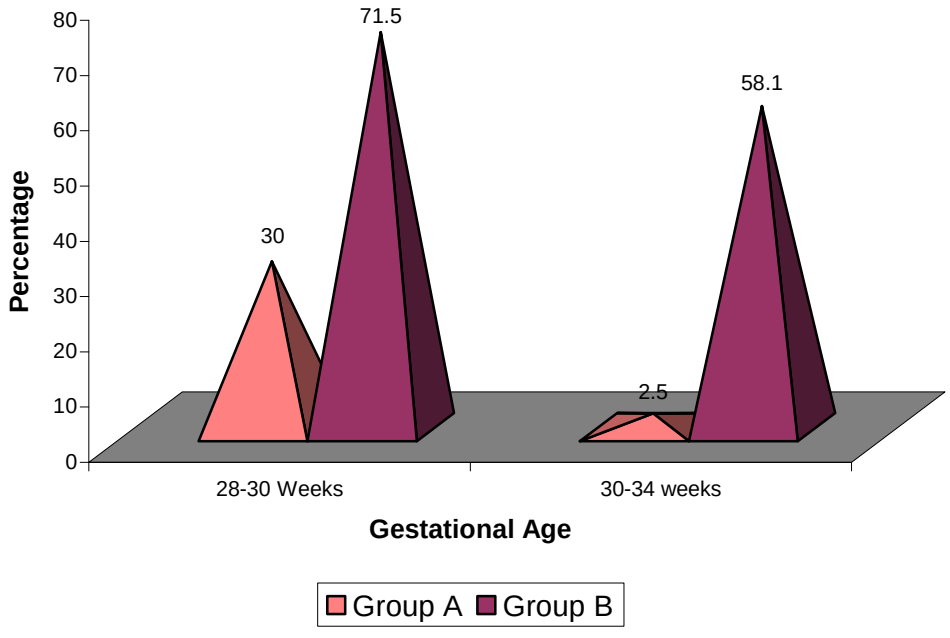
P value = 0.031

In 30-34 wks of Gestation, pregnancy was prolonged in 97.5% and 41.8% in case and control group respectively. In 28-30 wks of Gestation, pregnancy was prolonged in 70% in group A and 28.5% in group B. P value is 0.031 which is statistically significant.

RESPONSE ACCORDING TO GESTATIONAL AGE IN SUCCESS GROUP



RESPONSE ACCORDING TO GESTATIONAL AGE IN FAILURE GROUP



PROLONGATION OF PREGNANCY

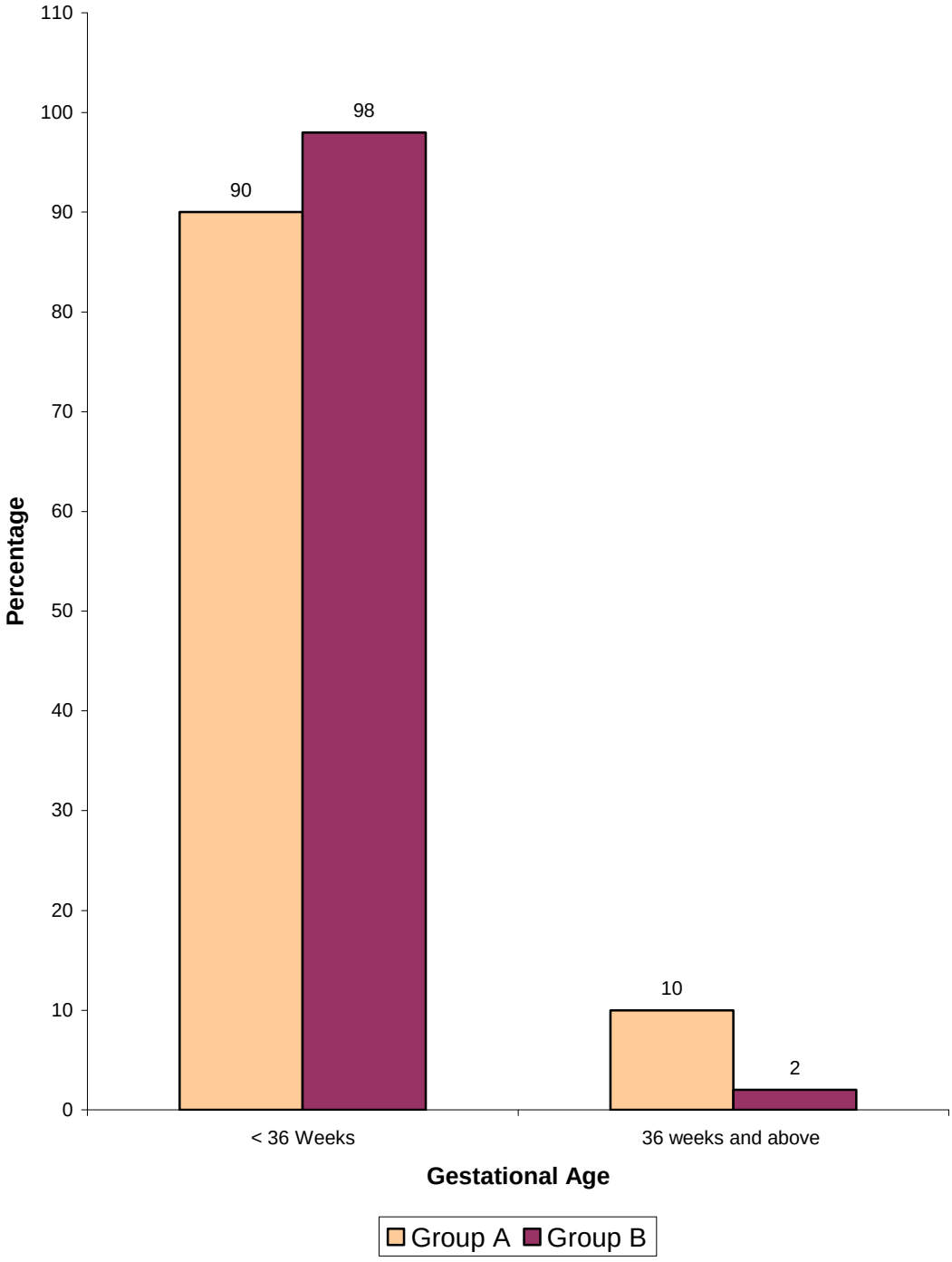
Table - 9

S. No.	Gestational Age	Group A		Group B	
		No.	%	No.	%
1.	<36 wks	45	90 %	49	98%
2.	>36 wks	5	10 %	1	2%

P value = 0.037

Pregnancy was prolonged to > 36 wks in 10% and 2% in group A and group B respectively. P value is less than 0.05.

PROLONGATION OF PREGNANCY



SUCCESS OF ACUTE TOCOLYSIS

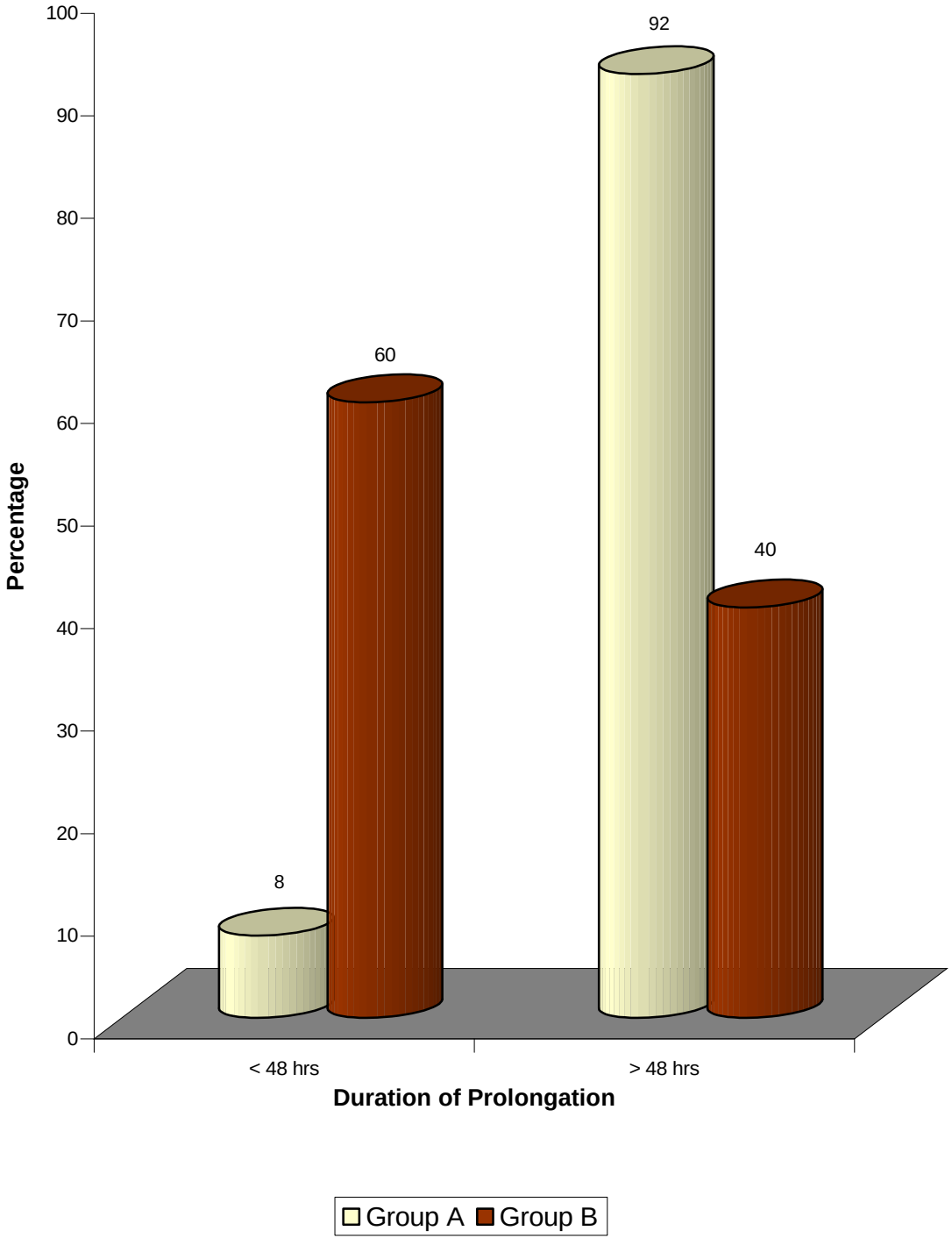
Table - 10

S. No.	Duration	Group A		Group B	
		No.	%	No.	%
1.	< 48hrs	4	8%	30	60%
2.	> 48hrs	46	92%	20	40%

P value = 0.014

The success of tocolysis in group A and group B were 92% and 40% respectively. P value was found to be 0.01 which is statistically significant.

SUCCESS OF ACUTE TOCOLYSIS



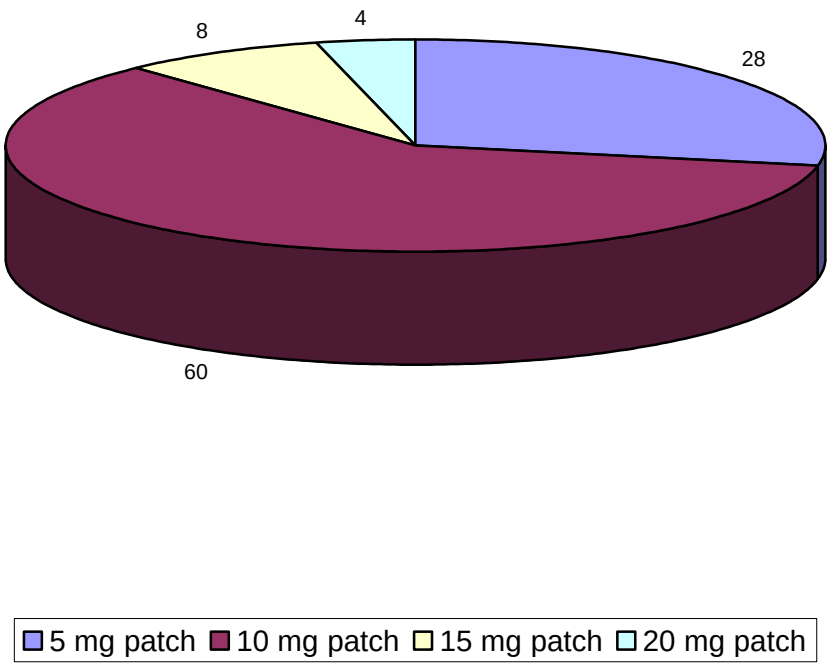
DOSAGE REQUIRED TO SUBSIDE CONTRACTIONS

Table - 11

S. No.	Drug Dosage to Subside Contractions	Group A	
		No.	%
1.	5 mg patch	14	28%
2.	10 mg patch	30	60%
3.	15 mg patch	4	8%
4.	20 mg patch	2	4%

In our study 4% of patients needed 20 mg patch, 8% needed 15 mg patch, 60% needed 10 mg patch and 28% of patients needed 5 mg patch to subside uterine contractions and there by to prolong labour.

DOSAGE REQUIRED TO SUBSIDE CONTRACTIONS



CERVICAL EFFACEMENT

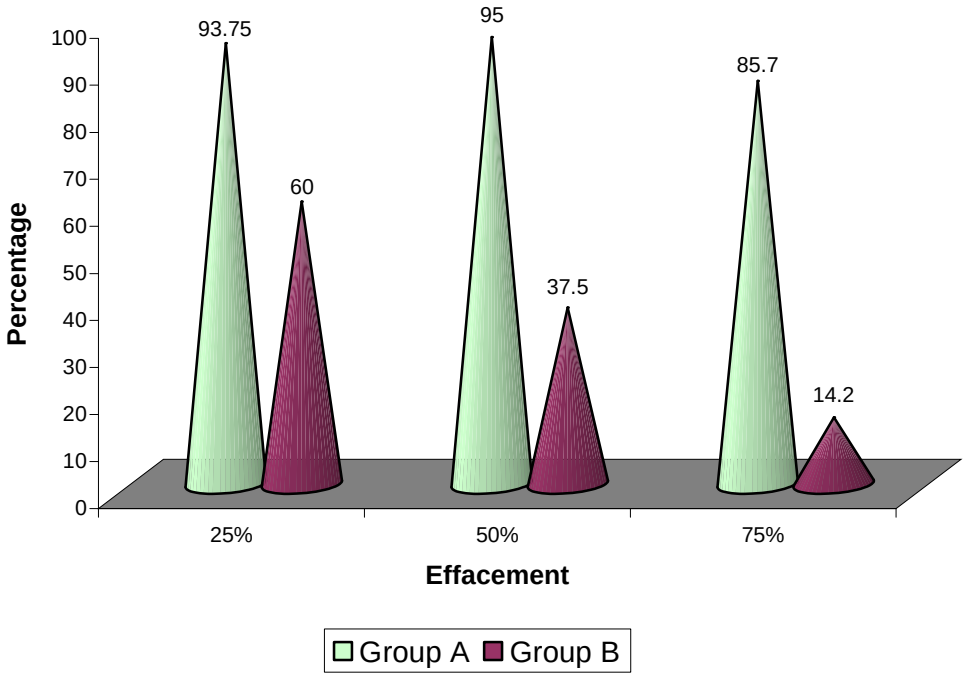
Table – 12

S. No.	Effacement	Group A		Group B	
		Success	Failure	Success	Failure
1	25	15(93.75%)	1(6.25%)	12(60%)	08(40%)
2	50	19(95%)	1(5%)	6(37.5%)	10(62.5%)
3	75	12(85.7%)	2(14.2%)	2(14.2%)	12(85.7%)

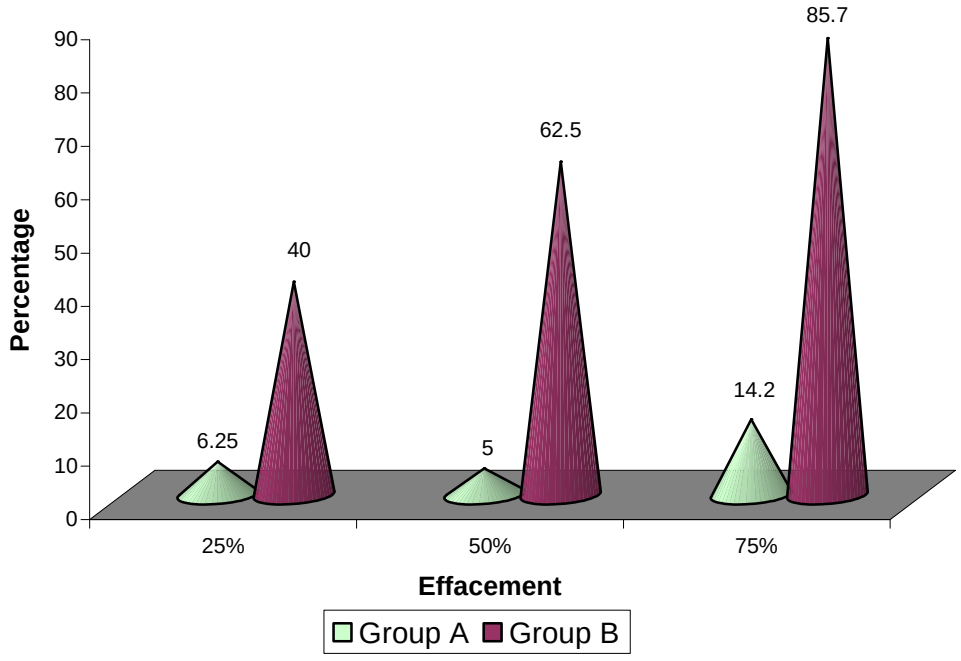
P value = 0.025

In patients with 25% cervical Effacement, 93.75% in Group A and 60% of patients in Group B showed prolongation of pregnancy. With 50% Cervical Effacement, successful tocolysis was observed in 95% of patients in Group A and 37.5% of patients in Group B. When the Cervix was 75% effaced, 85.7% in Group A and 14.2% in Group B had their pregnancy prolonged by more than 48 hours. P value is 0.025 and it is statistically significant.

CERVICAL EFFACEMENT IN SUCCESS GROUP



CERVICAL EFFACEMENT IN FAILURE GROUP



CERVICAL DILATATION

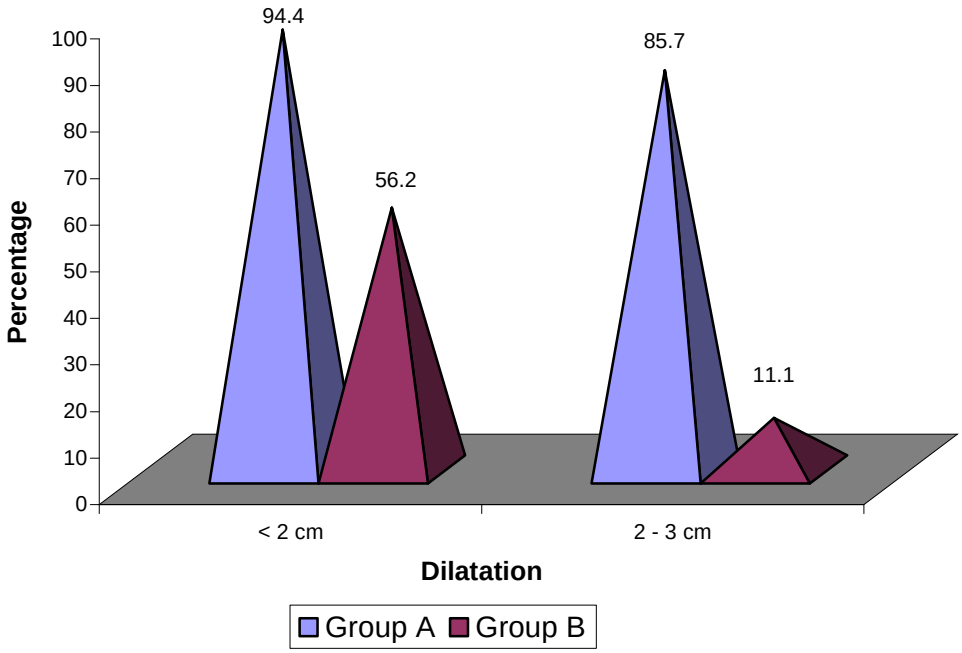
Table - 13

S. No.	Dilatation	Group A		Group B	
		Success	Failure	Success	Failure
1.	< 2 cm	34(94.4%)	2(5.5%)	18(56.2%)	14(43.7%)
2.	2 – 3 cm	12(85.7%)	2(14.2%)	2(11.1%)	16(88.8%)

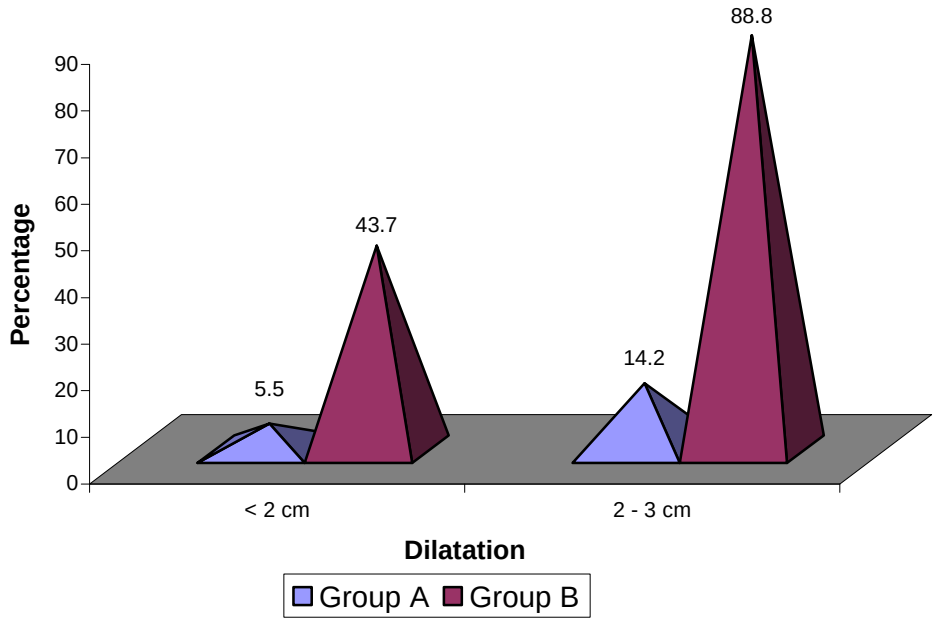
P value = 0.037

When the cervix was < 2 cm dilated, 94.4% in Group A and 56.2% in Group B had their pregnancy prolonged by > 48 hours. With 2-3cm cervical dilatation, prolongation of pregnancy was observed in 85.7% in Group A and 11.1% in Group B. P value is 0.037 (< 0.05) which is found to be statistically significant.

CERVICAL DILATATION IN SUCCESS GROUP



CERVICAL DILATATION IN FAILURE GROUP



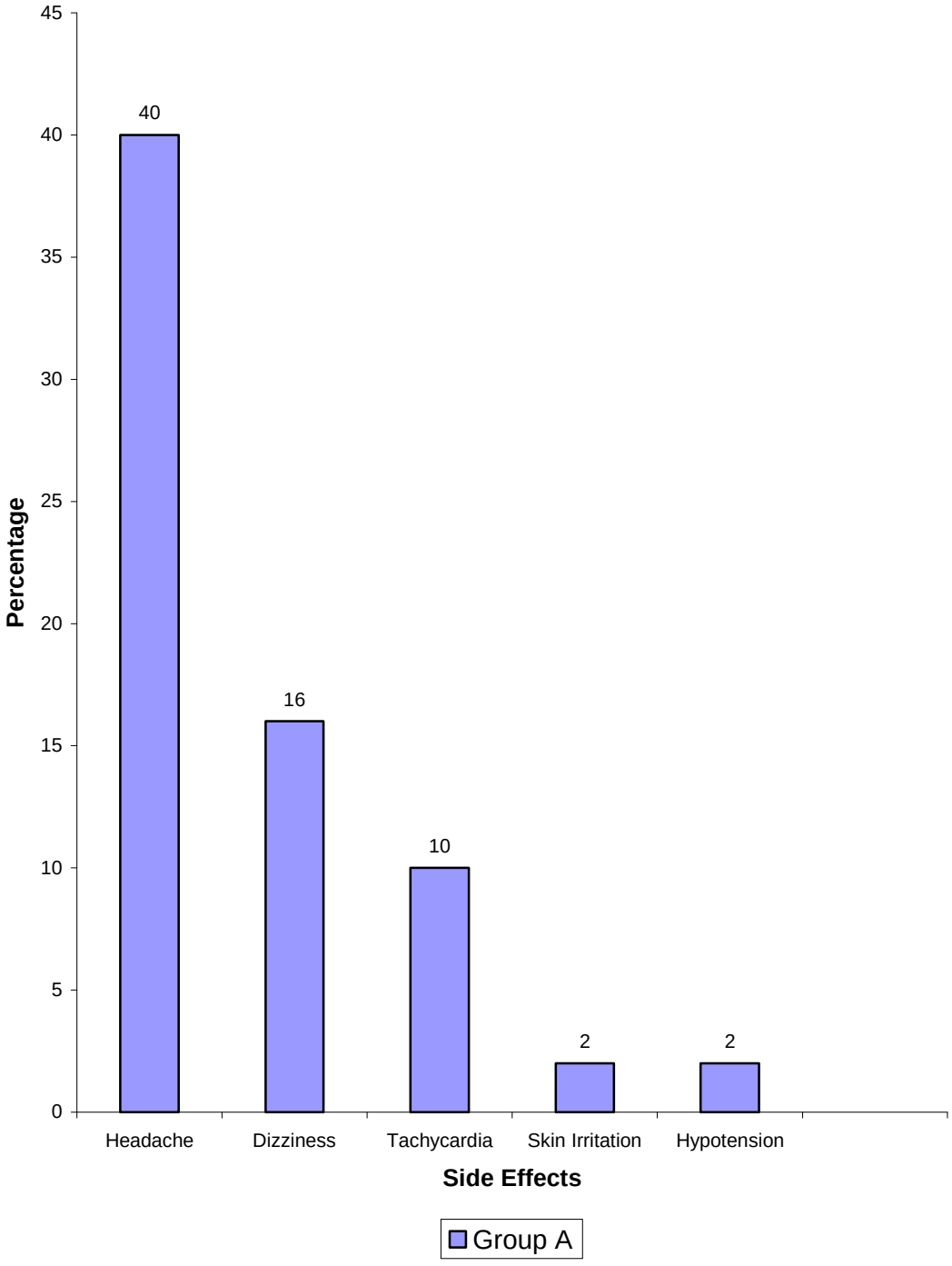
MATERNAL MORBIDITY AND MORTALITY

Table – 14

S. No.	Side Effects	Group A	
		No.	%
1.	Headache	20	40
2.	Dizziness	8	16
3.	Tachycardia	5	10
4.	Hypotension	1	02
5.	Skin Irritation	1	02

There was no maternal mortality. No case of postpartum hemorrhage was observed in those who delivered within 48 hours. The most common side effect observed among patients in group A was headache (40%).

MATERNAL MORBIDITY



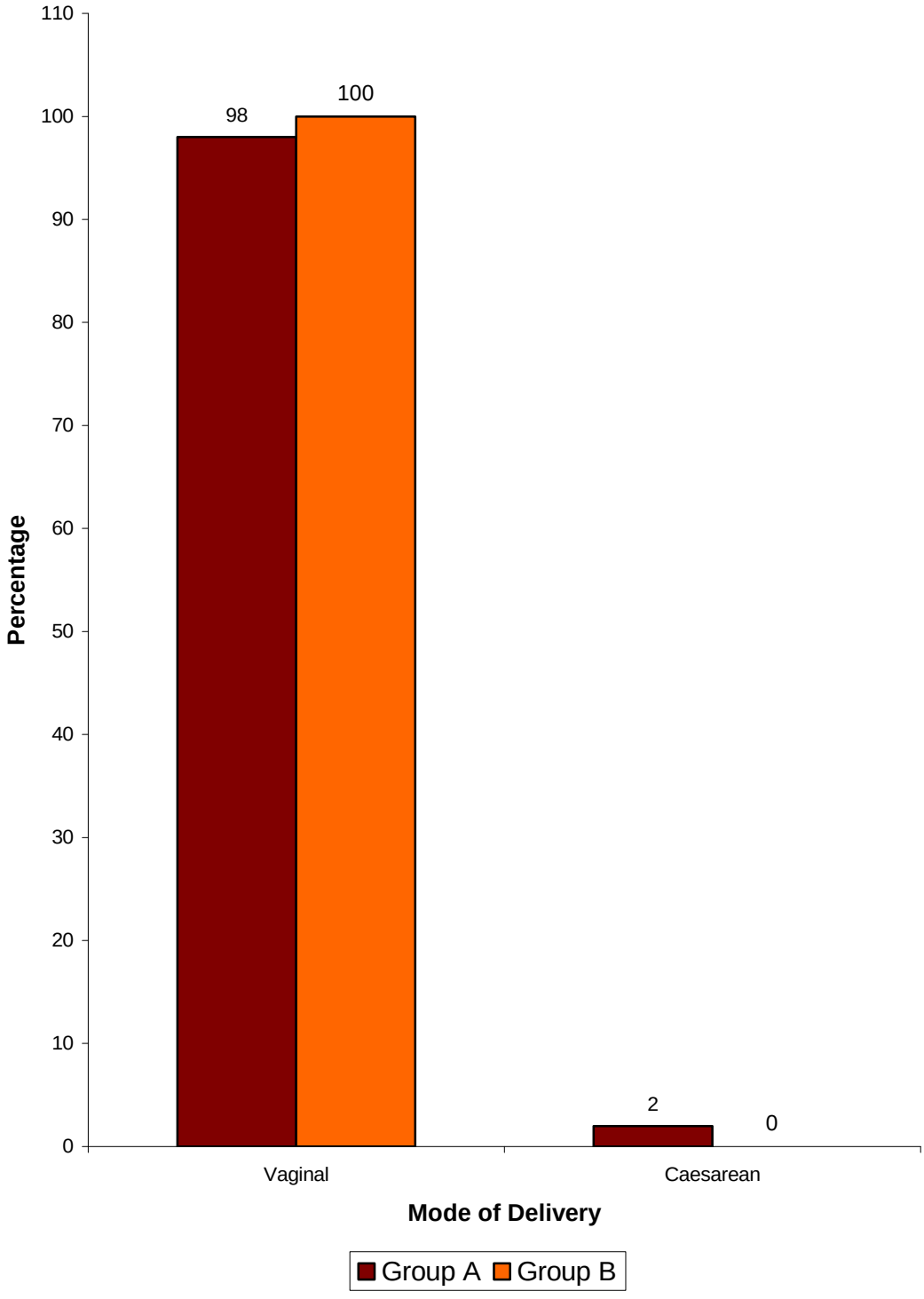
MODE OF DELIVERY

Table - 15

S. No.	Mode of Delivery	Group A		Group B	
		No.	%	No.	%
1.	Vaginal	49	98%	50	100%
2.	Caesarean	1	2%	-	-

98% and 100% of cases delivered vaginally in group A and group B respectively. One case of group A underwent Caesarean section for PROM with no response to Oxytocin.

MODE OF DELIVERY



NEONATAL MORTALITY

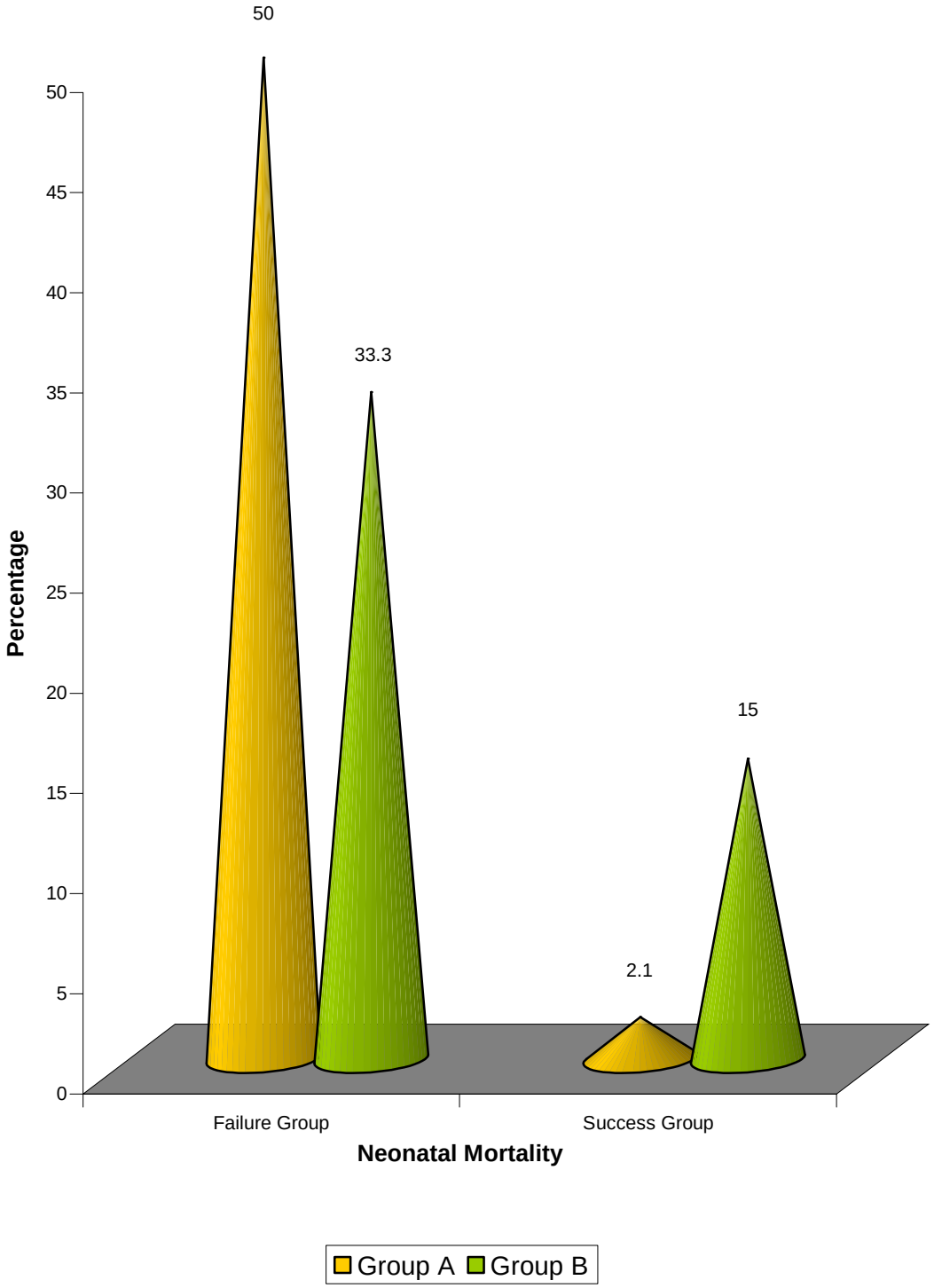
Table – 16

S. No.	Neonatal mortality among Babies born	Group A		Group B	
		No.	%	No.	%
1.	< 48 Hrs	02	50%	10	33.3%
2.	> 48 Hrs	01	2.1%	03	15%

P value = 0.04

Neonatal mortality was 50% in group A and 33.3% in group B among babies born in failure group whereas it is 2.1% in group A and 15% in group B among babies born in success group. Neonatal morbidity and mortality are primarily influenced by gestational age and thus maturity and less so by birth weight.[43] P value = 0.04 is statistically significant.

NEONATAL MORTALITY



NEONATAL MORBIDITY

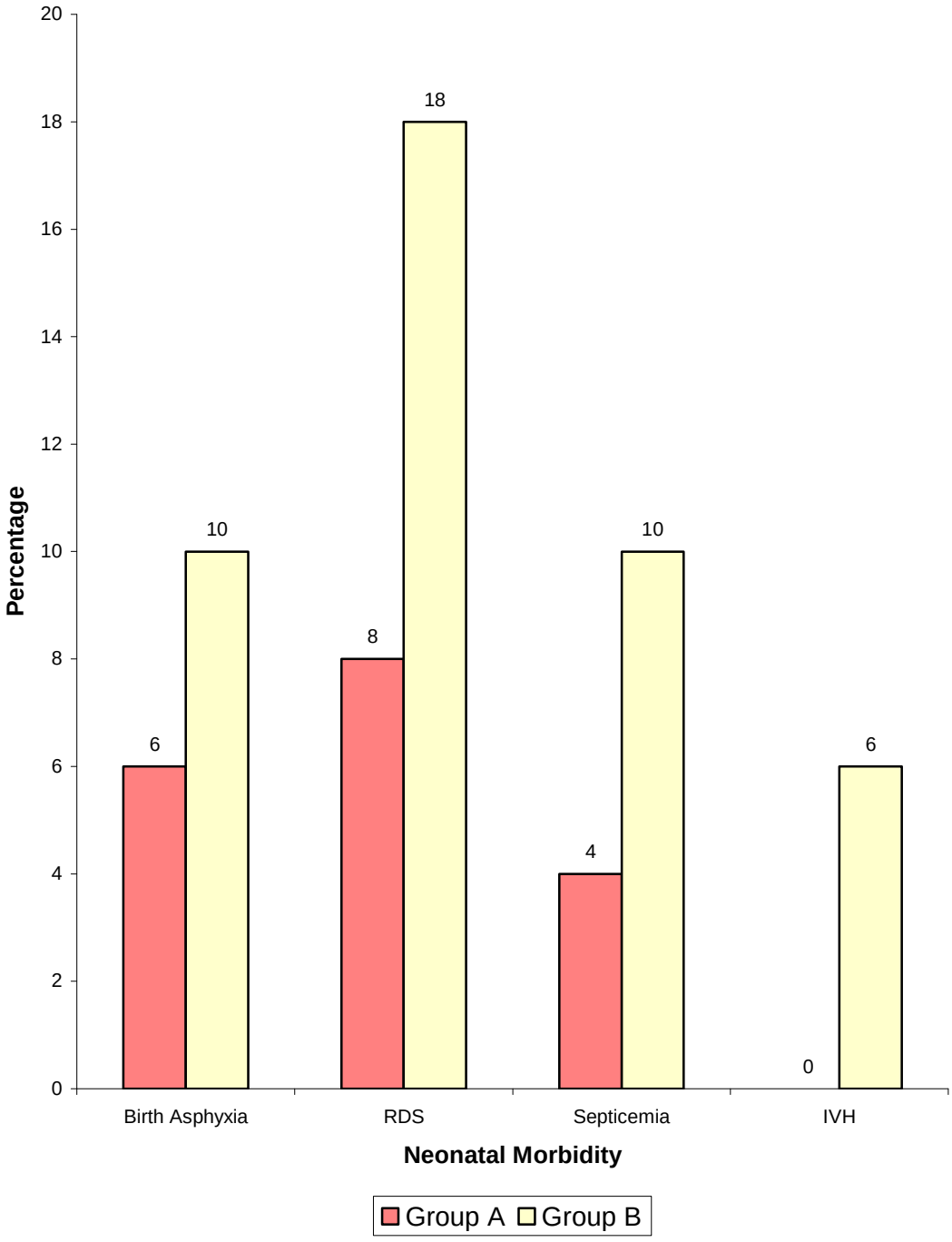
Table – 17

S. No.	Complication	Group A		Group B	
		No.	%	No.	%
1	Birth Asphyxia	3	06	5	10
2	RDS	4	08	9	18
3	Septicemia	2	04	5	10
4	IVH	-	-	3	06

P value = 0.014

RDS as a complication of prematurity is observed in 8% of babies in group A and 18% of babies in group B. The incidence of Birth Asphyxia is 6% in group A and 10% in group B. 4% of babes in group A and 10% in group B developed Septicemia. Intraventricular hemorrhage was observed in 6% of babies in group B. P value is 0.01 which is statistically significant.

NEONATAL MORBIDITY



APGAR SCORE

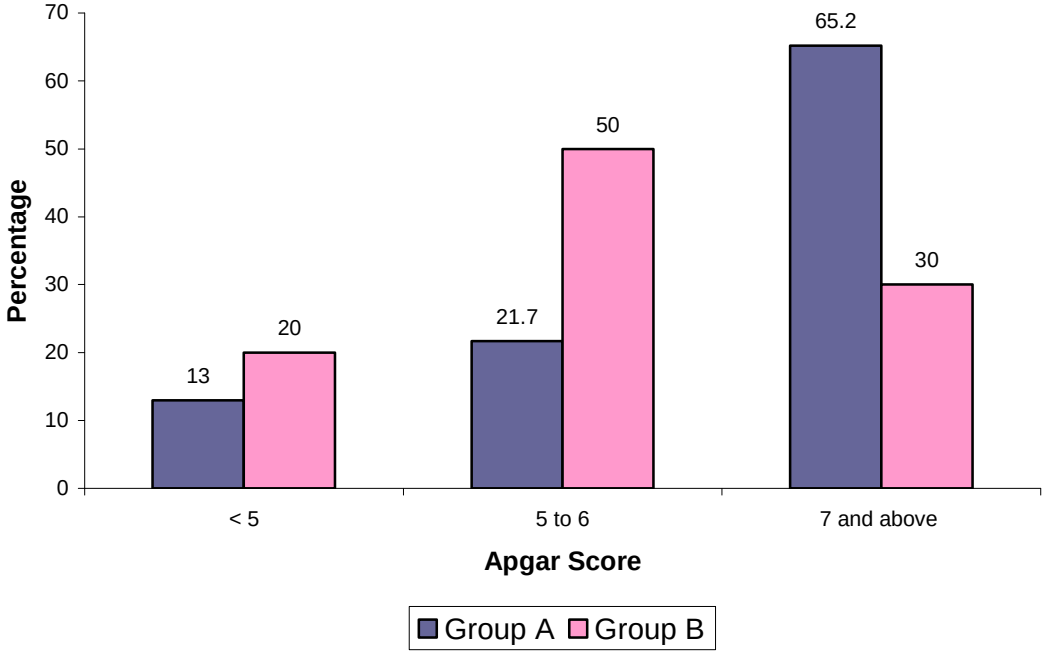
Table – 18

S. No.	Apgar	Group A Babies born in		Group B Babies born in	
		Success Group	Failure Group	Success Group	Failure Group
1	< 5	6 (13%)	2 (50%)	4 (20%)	18 (60%)
2	5 – 6	10 (21.7%)	1 (25%)	10 (50%)	11 (36.6%)
3	≥ 7	30 (65.2%)	1 (25%)	6 (30%)	1 (3.3%)

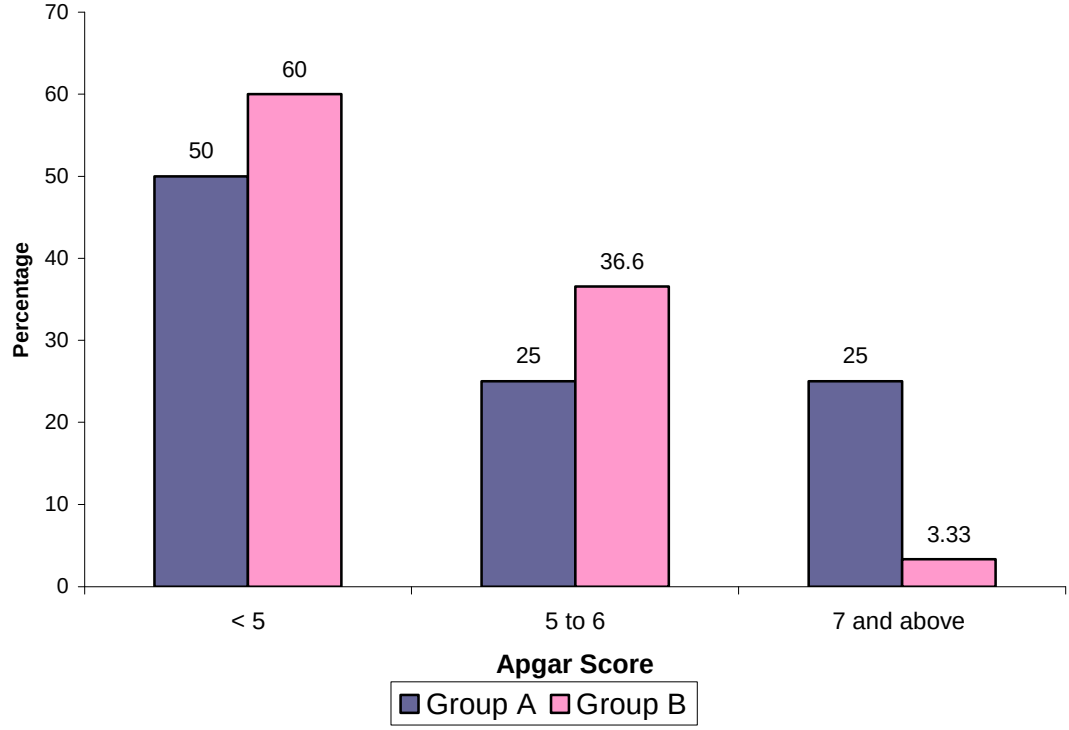
P value = 0.027

In group A 90.2% of babies had Apgar score of 7 and above where as only 33.3% of babies had Apgar score of 7 and above in group B.

Apgar Score among babies born in success group



Apgar Score among babies born in failure group



WEIGHT OF BABY AT BIRTH

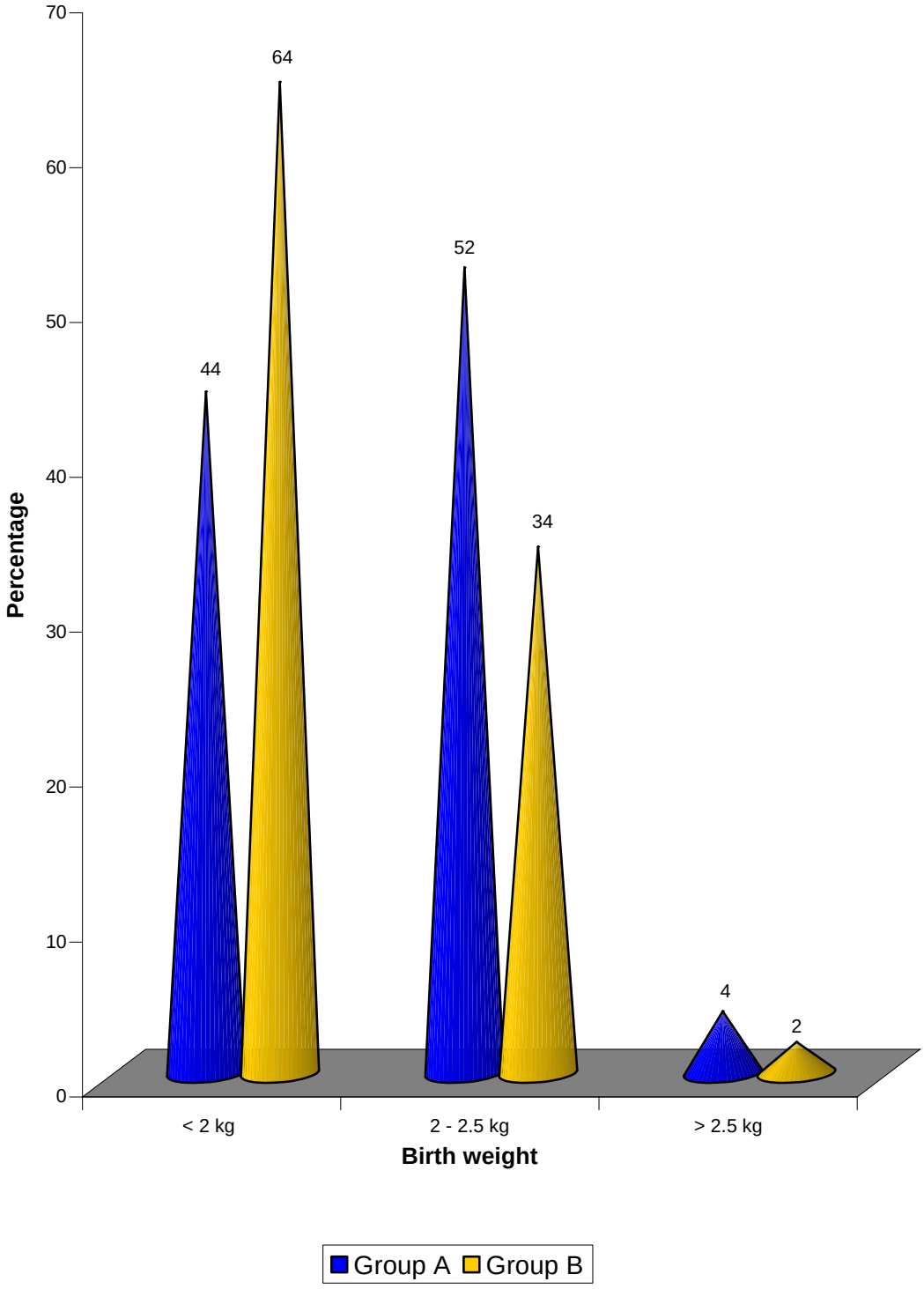
Table – 19

S. No.	Weight of the baby in Kg.	Group A		Group B	
		No.	%	No.	%
1.	< 2	22	44	32	64
2.	2 – 2.5	26	52	17	34
3.	> 2.5	02	04	01	02

P value = 0.0173

Most of the babies were born with a birth weight of 2 – 2.5 Kg. in group A (52%) where as in group B, most of the babies had birth weight of < 2 Kg. (64%). P value is < 0.05 which is statistically significant.

WEIGHT OF BABY AT BIRTH



DISCUSSION

DISCUSSION

On analysis of data, tocolysis with transdermal nitroglycerine is considered safe with good therapeutic efficacy.

When this data is compared to previous study, baseline characteristics did not differ significantly. In study by Lees *et al.*, multiparous women were more than primi and in age distribution most were in 25-29 years. Gestational age at entry differed considerably in each study group. Study by Lees *et al.* (1994) it was 24-36 weeks. In study by Krishna *et al.* (1996) Gestational age at entry varied from 18-34 weeks. Rowlands[44] (1996) in his study recruited patients with gestational age 16-32weeks. In Campbell study (1994) duration of pregnancy varied from 23-33weeks. In our study, patient recruited had Gestational age 28-34 weeks. Maximum no of patient were in 31-32 weeks of Gestation in Group A (46%) and in Group B (50%) were in 33-34 weeks of Gestation.

Cervical dilatation in our study range from 0-3 cm where as in study by Rowlands (1996) Cervical dilatation ranged between 2-8 cm. Campbell (1994) recruited patients in Cervical dilatation ranging from 0-4cm. Cervical dilatation influenced much on prolongation of pregnancy. When cervix is > 2 cm dilated tocolytic efficacy is minimal.

Lees (1994) Krishna *et al.* (1996) used10mg nitroglycerine patch where as Rowlands (1996) conducted study using 50 mg nitroglycerine patch. In study conducted here 60% needed 10 mg patch and 4% needed 20 mg patch. In Lees *et al.* (1994) study main side effect of nitroglycerine was headache (30%) and in our study it was 40%.

Success rate of acute tocolysis was 100% in study conducted by Krishna *et al.* (1996) for nitroglycerine. Lees (1994) showed success 95% for nitroglycerine as acute tocolysis. In this study conducted here, success rate was 92% for nitroglycerine.

Safety, efficacy, acceptability limits usage of drug. Transdermal nitroglycerine is considered to be a safer drug for its ease of use, easy metabolism with no side effect besides headache. While efficacy was studied, Transdermal nitroglycerine act as a good acute tocolysis for effective action of corticosteroid and to provide time for the patient to get transferred to tertiary neonatal care unit.

As a secondary analysis, an economic evaluation of trial was done. Both cost and consequence of treatment with nitroglycerine was evaluated. Though nitroglycerine patch was little costlier, but compared to patient care in neonatal unit & hospital stay, it is cost effective.

Nitroglycerine possible effect in delaying preterm delivery rate, good acute tocolytic efficacy, very minimal side effects, good neonatal

outcome makes the drug superior to other tocolytics. On complete analysis nitroglycerine is safe, easily applicable and acceptable by the patients.

Rapid & effective action obtained with nitroglycerine patch, its simplicity, safety suggest that nitroglycerine has a major contribution in the management of preterm labor.

SUMMARY

SUMMARY

In the randomized trial of Nitroglycerine patch in the prolongation of preterm labour, it was observed that.

1. Preterm labour was common in primigravida in the age group 20-24 years, belonging to lower socioeconomic status and who did not receive appropriate antenatal care.
2. There were 80% of cases between 30-34 weeks in group A and 86% in group B.
3. Previous preterm delivery was found in 12% in group A and 14% in group B.
4. 92% in group A and 90% in group B had cephalic presentation.
5. The success of Nitroglycerine patch as indicated by prolongation of pregnancy beyond 48 hrs was observed in 92% of cases compared with 40% in controls.
6. Nitroglycerine patch 10 mg was required in 60% of patients, 20 mg patch was required in 4% of patients to subside the uterine contractions.
7. In 30-34 weeks of gestation, success was observed in 97.5% in group A and 41.8% in group B. In 28-30 weeks, success rate was 70% and 28.5% in group A & group B respectively.

8. When the cervix was 25% effaced, successful tocolysis was observed in 93.75% of cases in group A and 60% in group B. When cervix was 50% effaced, prolongation of pregnancy beyond 48 hours was observed in 95% of patients in group A and 37.5% in group B. With 75% effacement, successful tocolytic effect seen in 85.7% in group A and 14.2% in group B.
9. When the cervix was < 2 cm dilated, prolongation of pregnancy beyond 48 hours was observed in 94.4% of cases in group A and 56.2% in group B. When the cervix was 2-3 cm dilated, successful tocolysis was observed in 85.7% and 11.1% of cases in group A and group B respectively. Mean duration of prolongation of pregnancy in Group A was 6.6 days.
10. Headache and dizziness were the commonest side effects observed in study group.
11. There was no maternal mortality in both the groups.
12. Neonatal mortality was due to complications of prematurity. Among success group, it was 2.1% in group A compared to 15% in group B.
13. The percentage of cases delivered vaginally in group A and group B were 98% and 100% respectively.

14. Apgar of ≥ 7% was observed in 90.2% of babies in group A and only 33.3% in group B.
15. Babies with Birth weight > 2 kg were delivered in 56% and 36% in group A and group B respectively.
16. The incidence of RDS in group A was 8% and in group B it was 18%. 4% of babies in group A and 10% of babies in group B had septicemia. Birth asphyxia was observed in 6% and 10% of babies in group A and group B respectively.

CONCLUSION

CONCLUSION

Labour inhibiting drugs may not treat the cause of preterm labour but they only treat the symptoms i.e. uterine contractions.

As these agents make the uterus refractory to stimuli for a short time the perinatal outcome is improved. In this clinical trial, the idiopathic spontaneous preterm labour whose onset was at 30 to 34 weeks of gestation had responded well to tocolytic therapy and neonatal outcome improved and no maternal mortality was observed. The maternal side effects were reversed on discontinuation of the drug. The drug had provided the fetus a valuable opportunity of being inside the mother's womb for a period enough to make the lungs mature by administration of exogenous steroids.

However decrease in the incidence of preterm labour lies in the identification of high risk patients, improving the socio-economic standard, better antenatal care, education and early detection of the onset of preterm labour.

On evaluation of transdermal nitroglycerine on acute tocolysis, it is found that nitroglycerine patch is absolutely safe and successful in achieving complete tocolysis.

Nitroglycerine is not only safe but also has a very minimal side effects like headache on mother. It has no untoward side effect on neonate. Neonatal outcome is good in all respects like apgar score, birth weight, less neonatal admission in nitroglycerine therapy.

To conclude transdermal nitroglycerine has a very good role to play as an acute tocolytic in the treatment of preterm labour and should be considered as first line drug of choice.

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PROFORMA

PROFORMA

NAME : AGE :

ADDRESS : IP NO :

DATE & TIME OF ADMISSION :

DATE & TIME OF DELIVERY :

DATE OF DISCHARGE :

OBSTETRIC CODE :

LMP :

EDD :

G.A :

BOOKED/UNBOOKED :

SOCIO ECONOMIC STATUS :

HISTORY OF PRESENT ILLNESS :

1. Lower abdominal pain
2. Vaginal discharge
3. Fever
4. Urinary tract infection
5. Bleeding pv
6. Draining pv
7. Coitus

MENSTRUAL H/O

MARITAL H./O

OBSTETRIC H/O:

Previous obstetric outcome

PAST H/O:

H/o preterm labour / Abortion – induced or spontaneous/ still birth

DM/ heart disease/hypertension/TB/Epilepsy/renal disease

PERSONAL H/O:

Smoker/Alcohol

GENERAL EXAMINATION:

- Pallor
- Oedema
- Febrile

VITALS:

- Temp :
- PR :
- BP :
- RR :
- Ht :
- Wt :

SYSTEMIC EXAMINATION

CVS :

RS :

CNS :

ABDOMEN:

P/A:

Symphysio fundal ht

Uterine size in wks

Presenting part

FHR

EFW

P/V:

Cervix :

- Effacement
- Dilatation
- Consistency
- Position

Station

Membrane

Pelvis

Draining pv/bleeding pv

Bishop score

INVESTIGATION:

Urine – sugar/ albumin/microscopy/culture sensitivity

Complete hemogram

Blood sugar

Blood urea

Vaginal swab c/s:

CTG:

USG:

- Singleton/multiple
- Vertex/breech
- G.A
- AFI
- Placenta
- Congenital anomalies
- EFW

GROUP A

GROUP B

TOCOLYTIC

BED REST

NTG PATCH

APPLIED ON

NO OF PATCHES

GROUP A : NITROGLYCERINE PATCH

TIME	DOSE	CONTRACTION	PR	BP	RR	FHR

COMPLICATIONS:

Headache

Tachycardia

Hypotension

Postural dizziness

Weakness

Skin rash

FETAL OUTCOME

Alive / Still Born :

Sex :

Mode of Delivery :

Birth Weight :

APGAR :

DELIVERED AT

28-30 WKS

30-32 WKS

32-34 WKS

34-36 WKS

> 36 WKS

TREATMENT DELIVERY INTERVAL

NEONATAL MORBIDITY: Admitted / Not

NEONATAL MORTALITY: Yes / No

: Cause

MASTER CHART

S. No.	Name	Age	IPNo	DOA	Group	Book status	Parity	H/O PTL	GA at entry (wks)	Presentation	Cx Eff %	Cx Dil	Station	Mat Comp	B.Wt in kg	GA at Del (wks)	DOP in days	Apgar	Neo outcome
1.	Tamilselvi	26	32934	31.7.08	B	UB	G2	-	34	C	50	2F	-3	-	2.1	34	1	6	
2.	Nirosa	19	33166	2.8.08	A	B	P	-	33	C	25	1F	-3	H	2.4	36	21	8	
3.	Vasanthi	27	33228	31.7.08	B	UB	G3	-	32	C	50	3Cm	-1	-	1.8	32	18 hrs	4	III
4.	Kala	27	33996	7.8.08	A	UB	G3	-	34	C	25	1F	-3	H	2.6	36	14	7	
5.	Danalakshmi	26	34229	9.8.08	A	UB	G2	-	32	C	75	1Cm	-1	H	1.5	32.2	2	6	
6.	Anjalaiden	28	34167	9.8.08	B	B	G2	+	34	C	75	3Cm	-1	-	2.2	34	5 hrs	8	
7.	Radha	28	34960	13.8.08	A	UB	P	-	34	C	50	2F	-2	H	2.3	35.1	8	8	
8.	Vijayalakshmi	22	35907	27.8.08	B	UB	G2	-	31	C	25	1F	-3	-	1.5	31	3	5	I
9.	Deepa	36	36223	23.8.08	B	UB	G2	-	34	C	50	2Cm	-1	-	2	34	12 hrs	6	II
10.	Tharamani	18	36346	25.8.08	A	B	P	-	31	C	25	1F	-3	-	2	33.6	20	8	
11.	Sathyalatha	22	36343	25.8.08	A	UB	G2	-	33	C	50	2F	0	H	2.2	34.5	12	8	
12.	Rani	36	36283	24.8.08	B	UB	G4	-	32	C	75	2Cm	-3	-	1.5	32	8 hrs	4	III, V
13.	Latha	21	36686	27.8.08	A	B	P	-	32	C	50	2F	0	BP¯	2	33.6	13	8	
14.	Umarani	26	36805	28.8.08	B	UB	G2	+	34	C	25	2F	-2	-	2.1	34	1	6	
15.	Tamilarasi	23	37208	30.8.08	A	UB	G2	-	34	C	50	2F	-2	H	2.6	36	14	8	
16.	Dilsath	28	37860	4.9.08	B	B	G3	-	31	C	50	2cm	-2	-	1.4	31	18 hrs	4	II, V
17.	Saheethabanu	26	38191	6.9.08	B	UB	G2	+	29	C	25	2F	-2	-	1.1	29	1	3	IV, V

18.	Pulalarasi	26	37886	5.9.08	A	B	G2	-	34	C	50	2F	-2	D	2.2	34.6	6	8	
19.	Dhanabakiyam	22	38759	10.9.08	A	UB	P	-	31	C	25	1F	-3	H	1.6	32	7	6	
20.	Jothi	21	39986	18.9.08	A	B	P	-	34	C	50	2F	0	H	2.5	36	14	8	
21.	Manjula	23	40227	20.9.08	B	B	G2	-	31	C	75	3cm	-1	-	1.4	31	5 hrs	4	III, V
22.	Rajeswari	22	40991	25.9.08	B	UB	P	-	32	C	50	2F	-1	-	1.5	32	1	4	II, V
23.	Sangeetha	27	40687	29.9.08	B	B	G2	-	29	C	25	1F	-3	-	1.1	29.2	2	3	III, V
24.	Rani	19	41451	28.9.08	A	B	P	-	32	C	25	1F	-3	D	2	33.5	12	8	
25.	Barakath	33	41523	29.9.08	B	UB	G3	+	34	C	75	3Cm	-1	-	2.3	34	4 hrs	6	
26.	Silambarasi	28	41680	29.9.08	A	UB	G3	-	34	C	25	1F	-2	S.I	2.2	34.5	5	8	
27.	Rajalakshmii	32	42283	3.1.08	B	UB	G3	-	32	C	75	3Cm	-1	-	1.6	32	6 hrs	4	I
28.	Saratha	23	42713	6.1.08	A	B	P	-	31	C	50	2F	-2	-	1.5	31.2	2	5	
29.	Kannammal	22	43122	9.1.08	A	UB	P	-	32	C	50	2F	-2	H	2	33.1	8	8	
30.	Sahayamary	33	43680	13.1.08	B	UB	G4	-	31	C	25	1F	-3	-	1.5	32	7	5	II
31.	Jayalakshmi	18	48323	14.1.08	A	B	P	-	30	C	50	2F	-2	-	1.4	31	7	5	
32.	Shinnammal	19	44825	23.1.08	B	UB	P	-	33	C	50	2F	-2	-	1.8	33.2	2	6	II
33.	Chitra	21	44393	19.1.08	A	UB	P	-	33	C	50	2F	-1	D	2.2	34	7	8	
34.	Ashrafnisha	18	45675	29.1.08	B	B	P	-	32	C	25	1F	-2	-	1.8	33.4	4	6	
35.	Ranjiitha	23	46593	31.1.08	A	B	G2	-	34	C	50	2F	-1	H	2.1	34.4	4	8	
36.	Chitra	22	46557	3.11.08	B	UB	P	-	29	Br	50	2Cm	-1	-	1.1	29	1	3	IV, V
37.	Patchiammal	18	48029	12.11.08	B	UB	P	-	32	C	25	2F	-2	-	1.6	32.4	4	5	I
38.	Sankiliyammal	18	49622	19.11.08	A	B	P	-	31	C	25	1F	-3	-	2	33	14	8	

39.	Rasia banu	21	47651	10.11.08	A	UB	P	-	34	C	25	2F	-1	-	2.5	36	14	9	
40.	Sangeetha	19	47435	25.11.08	B	UB	P	-	29	Br	50	2F	-1	-	1.1	29	1	3	I, V
41.	Kanagasundari	18	50509	27.11.08	A	B	P	-	30	C	50	2F	-2	-	1.3	30.4	4	4	
42.	Sudha	32	50518	27.11.08	B	UB	P	-	31	C	25	1F	-3	-	1.4	31.5	5	4	III
43.	Suganya	18	51506	5.12.08	B	UB	P	-	32	C	25	1F	-3	-	1.8	33.5	12	6	
44.	Jothi	23	51883	8.12.08	A	UB	G2	-	33	C	25	2F	-2	H	2.1	34	7	8	
45.	Gnanarani	27	52832	12.12.08	B	B	G2	-	34	C	75	2Cm	-1	-	2.2	34	5 hrs	6	
46.	Vanitha	26	53340	16.12.08	A	UB	G2	-	30	C	75	2Cm	-1	H	1.3	30.2	2	4	I
47.	Pitchiarani	28	104	1.1.08	B	UB	G2	-	34	C	25	1F	-3	-	2.1	34.6	6	8	
48.	Jeyabarathi	27	54686	26.12.08	A	B	G3	-	30	C	50	2F	-1	-	1.3	30.4	4	5	II
49.	Barani	28	909	7.1.08	B	B	G2	+	29	Br	50	2F	-1	-	1.2	29	1	3	II, V
50.	Valli	33	1038	8.1.08	A	UB	G4	-	32	C	25	2F	-2	D	2	32.6	6	8	
51.	Emalda	23	2259	19.1.08	A	UB	G2	-	34	C	75	2Cm	-1	-	2.1	34.2	2	8	
52.	Valliamal	26	3744	29.1.08	B	UB	G3	-	34	C	50	2Cm	-1	-	2.1	34	1	6	
53.	Benitharani	26	5265	9.2.08	A	B	G4	-	34	C	75	3Cm	-1	D	2.1	34.1	1	6	
54.	Thirumalai	28	5395	10.2.08	A	UB	G2	-	32	C	25	1F	-3	H	2.4	36	28	8	
55.	Rajakumari	28	680	18.2.08	B	B	G3	-	32	C	75	3Cm	0	-	1.6	32	6 hrs	4	
56.	Deepa	27	6783	19.2.08	A	UB	G3	-	34	C	25	2F	-2	D	2.1	34.3	3	8	
57.	Shanthi	27	6411	19.2.08	B	UB	G2	-	32	C	50	2F	-1	-	1.6	32.3	3	6	
58.	Selvi	33	6805	17.2.08	A	B	G3	-	32	Br	50	2F	-1	H	2	32.5	5	8	
59.	Parameswari	22	8163	19.2.08	B	B	P	-	34	C	75	2Cm	-1	-	2.1	34	6 hrs	6	

60.	Vijayalakshmi	264	10407	28.2.09	B	UB	G2	-	32	C	25	1F	-3	-	1.7	32.4	4	5	
61.	Kannaki	334	10965	13.3.09	A	B	G4	+	31	C	25	2F	-2	H	1.5	31.2	2	5	II
62.	Banupriya	27	12079	17.3.09	B	B	G2	+	29	C	50	2F	-1	-	1.2	29	1	3	I, V
63.	Nathiya	22	10708	24.3.09	A	UB	P	-	30	Br	75	3Cm	-1	-	1.3	30	12 hrs	4	I, V
64.	Dhowlath	22	12760	16.3.09	B	B	P	-	31	C	50	2F	-1	-	1.6	31.3	3	4	II, V
65.	Mariyammal	26	13306	28.3.09	A	UB	P	-	32	C	50	2F	-2	-	2	32.3	3	8	
66.	Jubaidha	22	13393	1.4.09	B	B	P	-	34	C	50	2F	-2	-	1.9	34	1	4	
67.	Dhanalaksmi	18	14122	1.4.09	A	B	P	-	31	C	75	3Cm	-1	-	1.5	31.2	2	7	
68.	Sharmila begam	23	14355	6.4.09	B	UB	G2	+	30	C	25	2F	-2	-	1.3	30	1	3	IV, V
69.	Basheera	36	14233	8.4.09	A	UB	G3	+	32	C	25	1F	-2	H	1.7	32.4	4	7	
70.	Vasantha	21	14726	7.4.09	B	B	P	-	34	C	25	1F	-3	-	2.6	36.2	16	9	
71.	Lakshmi	22	14752	10.4.09	B	UB	P	-	34	C	50	2F	-1	-	1.9	34	2	2	
72.	Malathi	23	15010	10.4.09	A	B	P	-	33	C	50	2F	-1	D	1.8	33.5	5	8	
73.	Maheswari	22	15122	12.4.09	A	UB	P	-	21	C	75	2Cm	-1	T	1.7	32.2	2	7	
74.	Aruna	23	15992	13.4.09	B	B	P	-	34	C	50	2F	-1	-	1.6	34	1	4	
75.	Banumathi	36	16825	19.4.09	A	B	G3	+	31	C	25	1F	-3	H	1.8	32.1	8	7	
76.	Poongothai	21	17047	24.4.09	B	B	P	-	31	C	25	2F	-2	-	1.4	31.3	3	4	II, V
77.	Maria Anthoniyammal	23	16519	25.4.09	A	UB	G2	+	29	C	50	2F	-2	-	1.1	29.2	2	3	II, V
78.	Alagu	21	17088	22.4.09	B	UB	P	-	33	Br	75	3Cm	0	-	1.5	33	6 hrs	4	II, V
79.	Anandhi	18	17229	22.4.09	A	B	P	-	32	C	75	3Cm	-1	-	1.5	32	1	7	
80.	Kokila	22	18102	27.4.09	B	B	P	-	34	C	25	1F	-2	-	2.2	35.3	10	8	

81.	Banumathi	21	18052	2.5.09	A	UB	P	-	34	C	75	2Cm	-1	H	2.1	34.2	2	7	
82.	Sornam	22	18163	2.5.09	A	B	P	-	29	C	50	2F	-1	D	1.3	29.6	6	3	III
83.	Kalaiselvi	23	19567	3.5.09	B	UB	P	-	34	C	25	1F	-3	-	2.3	35.1	8	8	
84.	Nirmaladevi	22	20212	11.5.09	B	B	P	-	34	C	75	3Cm	-1	-	2.1	34	5 hrs	6	
85.	Ariamala	23	20667	14.5.09	A	UB	P	-	30	C	75	3Cm	-1	T	1.3	30.2	2	4	II
86.	Nathiya	23	21314	18.509	B	UB	P	-	33	Br	25	2F	-2	-	1.9	33.3	3	6	
87.	Saguntala	22	22963	22.5.09	A	UB	P	-	22	Br	75	2Cm	-1	H	2	32.2	2	5	
88.	Kavitha	21	24967	1.2.09	B	B	P	-	34	C	25	1F	-3	-	1.5	34.3	3	7	
89.	Rasathi	23	24929	13.6.09	A	UB	G2	+	30	C	75	3Cm	-1	D	1.2	30	1	4	III, V
90.	Shanthi	22	25680	13.6.09	B	UB	P	-	34	C	75	3Cm	-1	-	2.1	34	5 hrs	6	
91.	Thenmozhi	21	25691	13.6.09	A	B	P	-	31	C	25	1F	-3	H	2.1	34.2	23	8	
92.	Muthulakshmi	23	27778	21.07.09	B	B	P	-	34	C	25	1F	-2	-	2.2	34.3	3	8	
93.	Gomathi	21	31866	28.7.09	B	UB	P	-	34	C	75	3Cm	-1	-	2.1	34	6 hrs	6	
94.	Revathi	22	34261	7.8.09	A	UB	P	-	32	Br	75	3Cm	-1	H	1.6	32.2	2	6	
95.	Sumathi	23	34218	6.8.09	B	B	G2	-	32	C	75	2Cm	-2	-	1.6	32	6 hrs	4	
96.	Ranganayaki	23	34335	7.8.09	A	UB	P	-	32	C	75	2Cm	-1	-	1.4	32.2	2	5	
97.	Veeranagammal	22	35048	11.8.09	B	B	P	-	34	C	25	2F	-1	-	2.2	34	1	6	
98.	Durgadevi	24	35076	12.8.09	A	B	G2	+	30	C	50	2F	-2	H	1.3	30.4	4	4	I
99.	Ilakya	21	35321	13.8.09	B	B	P	-	33	C	75	3Cm	-1	-	1.8	23	6 hrs	4	
100.	Kavitha	24	35908	18.8.09	A	UB	P	-	32	C	75	3Cm	-1	-	1.5	32.2	2	5	

ABBREVIATIONS

DOA	-	Date Of Admission	Br	-	Breech
Cx Eff	-	Cervical Effacement	H	-	Headache
Cx Dil	-	Cervical Dilatation	D	-	Dizziness
Mat Comp	-	Maternal Complication	BP	-	Hypotension
B.Wt	-	Birth Weight	S.I	-	Skin Irritation
GA at Del	-	Gestational Age at Delivery	T	-	Tachycardia
DOP	-	Duration of Prolongation	I	-	Birth Asphyxia
Neo	-	Neonatal	II	-	Respiratory Distress Syndrome (RDS)
UB	-	Unbooked	III	-	Septicemia
B	-	Booked	IV	-	Intraventricular Hemorrhage
C	-	Cephalic	V	-	Fetal Death